INNOCENT AND MALIGNANT TUMORS

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THE ESSENTIAL SIMILARITY OF INNOCENT AND MALIGNANT TUMOURS

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ESSENTIAL SIMILARITY OF INNOCENT AND MALIGNANT TUMOURS

A STUDY OF TUMOUR GROWTH

BY

CHARLES W. CATHCART

M.A., M.B., C.M.(EDIN.), F.R.C.S.(ENG. AND EDIN.)

SURGEON, ROYAL INFIRMARY, EDINBURGH

FORMERLY CONSERVATOR OF THE MUSEUM OF THE ROYAL COLLEGE OF SURGEONS, EDINBURGH

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Dedicated

TO

LORD LISTER

BY HIS GRATEFUL PUPIL

THE AUTHOR

PREFACE

In the pages which follow, I have somewhat extended the two Lectures on the "Essential Similarity of Innocent and Malignant Tumours" which I delivered in March 1904 to the Fellows of the Royal College of Surgeons, Edinburgh. An abstract of the Lectures was published in the *British Medical Journal* in June of the same year, and I have wished to publish an account of the argument in full, although unable to do so until the present time.

The illustrations of the three Selected Gradation Series are, with very few exceptions, "process" reproductions of photographs taken directly from specimens. The source of the specimen is in every case indicated, but I desire here to express my thanks to those who have allowed me to utilize the various specimens for my present purpose—*i.e.*, To the Museum Committee of the Royal College of Surgeons, Edinburgh; to the Council of the Royal College of Surgeons of England; to Professor D. J. Cunningham, Keeper of the Anatomical Museum of the University of Edinburgh; to Professor G. S. Woodhead, Curator of the Humphry Museum, University of Cambridge; to Professor Chiene and to Mr. J. Hodsdon, of Edinburgh; and to Dr. Whiting, of London.

The Photomicrographs were all taken with a low power of the microscope—magnified in most cases 75 diameters, in a few cases 50 diameters.

CHARLES W. CATHCART.

Edinburgh, *January* 1907.

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CHAPTER I

INTRODUCTORY—MALIGNANCY AND ITS VARYING DEGREES

ABOUT ten years ago, when engaged in preparing a new Catalogue of the specimens in the Museum of the Royal College of Surgeons of Edinburgh, I dealt with tumour specimens by first forming various groups, each composed of tumours which had arisen in the same organ or tissue. These groups I tried to divide into the usual sub-groups of innocent and of malignant individuals, but found that, while it was easy to select out of every group typically innocent and typically malignant specimens, a large number always remained over, which did not properly belong to either of the intended sub-groups. After this method had been tried for some time, with no improvement resulting from increased practice and experience, I gave it up, and adopted the following. The tumours arising in the various organs or tissues were taken together as before, on the basis of their general resemblance to one another in structure, but now instead of being separated into innocent and malignant sub-groups, they were arranged in order of their malignancy, beginning with the innocent forms and ending with the malignant. The intermediate forms were used to bridge over the interval between the two extremes. The absence of a clinical history in the case of some of the specimens, and the imperfect preservation of a large number, made the task of arrangement more difficult than it would have been otherwise, but, on the whole, the result was much more satisfactory than that of the former method. This favourable opinion was strengthened as the work extended and progressed.

Among pathologists, the question as to the relation which may or may not exist between innocent and malignant tumours is by no means settled. Many authorities hold that cancers (including also other forms of malignant growth) form a class by themselves. Others think that all forms of tumour growth are essentially similar, whether they be clinically innocent or malignant. Not a few pathologists, however, have been unable to make up their minds upon the subject: hence there seems to be room for further discussion. I hope that by bringing together arguments in favour of the "essential similarity" view, I may not only establish what I believe to be an important truth in pathology, but may also help to direct the search for a cure for cancer into paths which are more likely to lead to success than those which start from a misconception of the nature of that disease.

Since the terms "innocent" and "malignant" are so intimately bound

up with this discussion, it is necessary that we should try at the outset to grasp their meaning when applied to tumours. The contrast between a characteristic example of each class of tumour is well expressed by Mr. Bland Sutton when he says, "The baneful effects of innocent tumours depend entirely upon their environment, but malignant tumours destroy life whatever their situation."

If, now, we try to see *how* it is that malignant tumours destroy life whatever their situation, we shall find that they produce their evil effects differently in different cases. It may be

(*a*) *By excessive local growth*, whereby the tumour absorbs for its own use nutriment which would otherwise have supplied the normal tissues;

(*b*) *By degeneration and hæmorrhage*, whereby the blood is deteriorated and wasted;

(*c*) *By local dissemination*, in which case the tumour sends offshoots into the surrounding tissue at a little distance from itself. These offshoots form new centres of growth, and thus act like an excessive overgrowth of the original focus in exhausting the patient;

(*d*) *By infiltration of the surrounding tissues*, the tumour invading and destroying all the structures which it touches;

(*e*) *By lymph dissemination*, whereby new foci of growth are carried by the lymph vessels to the adjacent glands, where they stop and begin work afresh;

(*f*) *By blood dissemination*, whereby the blood is the agent by which the foci are distributed to different parts of the body.

These various ways of causing death may not be all present in the same case. Those which have been placed first are associated with the less malignant forms of tumour, and those at the end of the list with the more malignant forms. The less malignant manifestations are more frequently present alone, while the others are more frequently combined. Thus local growth may destroy life without any form of dissemination, but if local infiltration occurs, dissemination by the blood- or lymph-stream is generally present also.

One well-known practical test of malignancy is "return after removal." This, of course, means return after the removal of all visible portions of the tumour. Such return is an outcome of what has just been described as local dissemination, infiltration, or dissemination by blood- or lymph-stream. It depends on the power of the cells to break free from the original focus and to develop a fresh mass of tumour growth when carried to a new part of the patient's body. "Return after removal," therefore, is not an additional manifestation of malignancy; only an unfortunate way of clinically proving that certain malignant features have undoubtedly been present in a particular case.

In contrast with "malignant" tumours, those which are "innocent" may be said to have characters negative to those of the malignant forms. A typically innocent tumour does not injure its host's life by excessive growth, it does not infiltrate the tissues which surround it, and it does not give rise to new tumours either by "local dissemination" or at a distance, when carried by the blood- or lymph-stream. While, however,

it is possible to say all this of some tumours, there are others in which the line of demarcation between the innocent and malignant characters is not a sharp and well-defined one. In other words, the two classes of tumour are not distinct, but differ only in degree.

There are, in my opinion, three features of the character and structure of tumours to which, in this connection, the attention of pathologists has not been sufficiently drawn :—

I. *A Gradation in Character from Innocent to Malignant which can be demonstrated.* The specimens selected to illustrate this aspect of the nature of tumours must, of course, be taken from different individuals.

II. *A Transformation in Character from Innocent to Malignant which may sometimes be observed in the same tumour.*

III. *Certain Combinations of Character which may sometimes be observed.* Thus tumours which in almost all particulars have the characters of an innocent tumour, may yet manifest certain characters which are recognized to belong properly to malignant forms.

In the pages which follow, I hope to be able to make clear these three features of tumour growth.

CHAPTER II

GRADATION IN CHARACTER FROM INNOCENT TO MALIGNANT

THE view that malignant characters are present in different degrees in different individual tumours of a similar kind may, I think, be supported in two ways: (1) By the presentation of one or more series of similar tumours which have been arranged in order, beginning with innocent and ending with malignant forms; (2) by reference to the published opinions of various pathologists who have observed this gradation in one or more tumour groups. The first way gives the reader material to judge of the argument for himself; the second lends to the argument the support of many independent and capable witnesses, and indicates that the gradation method can be applied to other kinds of tumour than those which I have selected for illustration.

The tumours here selected for illustration in series are those arising in bone, since this kind of tumour lends itself peculiarly well to illustration by photography. The photographs are mostly taken directly from specimens. In each case the source of the specimen is mentioned. Where no clinical history is given, it is to be understood that none is available.

Tumours arising from bone have been arranged in three groups—

1. Cartilaginous tumours;
2. Bony tumours arising from the bone and periosteum and composed of this type of tissue;
3. Medullary tumours arising from the medulla and resembling it in structure.

In each group, the series begins with innocent and ends with malignant forms.

I.—FIRST GRADATION SERIES: CARTILAGINOUS TUMOURS.

(1) *Chondromata growing slowly on the Metacarpal Bones of the Thumb and Forefinger.*

The specimens from which the photograph (Fig. 1) was taken, belonged originally to Sir Charles Bell, and are now in the Museum of the R.C.S.Ed. (6. 361.)

> "The patient, when a boy, had his hand crushed, and afterwards the tumour formed gradually."

"The sections show that the tumours are composed of numerous small lobules of hyaline cartilage, each apparently surrounded by a very delicate stroma. Some of the nodules seem to have been softening. The surface of each tumour is formed by a thin layer of bone continuous with the bone from

which the tumours have grown. Imperfect and irregular appearances of septa are seen here and there passing inwards from the interior of the bone shell."

In all probability these tumours were removed solely on account of their mechanical interference with the usefulness of the hand.

(2) *Ossified Chondroma involving two of the Metacarpal Bones.*

The specimen from which this photograph (Fig. 2) was taken is in the Anatomical Museum of the University of Edinburgh (Os. D. p. 13). It was partially macerated, then dried.

There is no clinical history attached to this specimen; but it may be taken as an example of the chondromata, which become ossified and remain quiescent, and which are only removed on account of their unsightliness or mechanical inconvenience.

(3) *Chondroma of the Humerus of ten years' growth; removal by Amputation of entire Upper Limb; no return.*

The specimen from which the photographs (Figs. 6, 7) were taken was presented to the Museum of the R.C.S.Ed. by Sir T. Chavasse of Birmingham. (6. 354).

> "The patient, a man, æt. 40 (Fig. 3), had noticed the tumour growing below and external to the shoulder-joint for ten years before he consulted Mr. Chavasse. It had grown steadily, and by its increase had caused pain in his neck and forearm. During the last eighteen months the growth had been more rapid, and the surface had become irregular. Three months before the operation, softened patches had appeared at the lower part. One of these had given way, and an oily fluid had at first drained from it; but shortly before the operation free hæmorrhage, apparently venous, had occurred from it also. Up to the last the affected arm, with the aid of a sling, was used for driving, and there was no deterioration of the patient's general health."
>
> "The upper limb, including the scapula and part of the clavicle, was removed by Mr. Chavasse, according to Berger's method, in January 1889. The patient made an excellent recovery (Fig. 4), and in 1905—sixteen years afterwards—was known to be in excellent health."

The weight of the specimen after the operation (Fig. 5) was twenty-one pounds, of which about eighteen pounds would belong to the tumour. The circumference of the tumour at the widest part was twenty-eight inches. Its consistence was firm and elastic, except at one or two spots where it had become cystic. The outline was nodular, and several large veins were seen on the surface. In cutting the tumour, calcareous nodules were met with, so that the knife and saw had to be used alternately.

The tumour consists of nodules of cartilage varying from the size of a pea to that of a walnut (Fig. 7). The smaller nodules, when fresh, were translucent and firm, like the substance of the crystalline lens. The large ones were yellowish and somewhat opaque, and in some cases had softened at the centre. Round the nodules there was a delicate stroma of connective tissue, carrying blood-vessels. From these, in some places, lime salts have been deposited so as to form a calcareous shell round the nodules. Here and there, where several calcareous nodules have united, the interior is

transformed into cancellous bone. The outer part of the shaft of the humerus is thickened and sclerosed at the upper end, but the interior is unaffected. The tumour seems to have started from the thickened part, and to have partially surrounded the humerus.

Microscopically (Fig. 6), the tumour was found to consist of hyaline cartilage without special features.

For further particulars of this case, see "Successful Removal of the Entire Upper Extremity for Osteo-Chondroma," by Thomas F. Chavasse, M.D., etc., in vol. lxxiii. of the *Medico-Chirurgical Transactions of London.*

(4) *Chondroma of Humerus, growing more rapidly than the preceding one.*

The wax model from which the photograph (Fig. 9) was taken is in the Museum of the R.C.S.Ed. (6. 357).

The patient was under the care of the late Professor Syme.

Six years before the operation the patient had occasional pains in the shoulder, and six months afterwards he observed on the forepart of the shoulder a firm swelling, which appeared to be seated on the bone. Three years later he fell and broke the affected humerus about the middle, but it united without displacement. "But the morbid growth advanced more rapidly after the injury, and his uneasy sensations kept pace with its progress. He said that what chiefly distressed him latterly, was a feeling of weight and oppression which never ceased, and was particularly severe during the night. He had no other complaint, and seemed to be sound in all other respects."

Before the operation (Fig. 8) the following description was drawn up (Syme's *Contributions to the Pathology and Practice of Surgery*, 1848, p. 108):—"It had a very broad base, which completely filled the axilla, and seemed to grow out from the side of the thorax. The shoulder-joint did not admit of any motion, but the arm moved freely along with the scapula. The head of the humerus seemed to be the centre of the swelling, which extended from it in every direction, terminating about half-way from the elbow, and approaching within two inches of the sternum. The clavicle and spine of the scapula could be traced nearly, but not quite, to their junction. The consistence of the tumour was extremely firm, feeling in some parts as if it were composed of bone, and in others of fibro-cartilage. The surface appeared in general pretty equal, but when examined more carefully was found to be irregularly nodulated. The colour of the integuments was not altered."

The tumour was removed, along with the glenoid cavity, and the acromion and coracoid process of the scapula, and part of the clavicle. The patient made an excellent recovery. The tumour (Fig. 9) weighed twelve pounds. It was macerated, but all the parts fell to pieces.

Writing about eleven years after the operation, Mr. Syme said: "I heard little of the patient, who continues well."

Mr. Syme called it a fibrocartilaginous tumour. The acromion and coracoid processes, and the glenoid cavity, were removed along with the tumour, not because they had been invaded by the growth, but because their removal facilitated the operation.

This has probably been a case like the previous one; and the nodular character of the cast further confirms this view.

This tumour has been placed further on in the scale towards malignancy than the last, because of its more rapid growth. It had on this account caused more inconvenience.

(5) *Chondromyxoma of Thumb, following injury seven years previously. Steady growth for three years. Amputation; local return; removal; no further recurrence. Patient well fifteen years after amputation of thumb.*

The specimen and the cast from which the photographs (Figs. 10, 11, 12) are taken are in the Museum of the R.C.S.Ed. (6. 365; 6. 366).

"The man, æt. 51, was admitted to the Royal Infirmary, Edinburgh, in December 1891. His family history was good, and he had previously been quite healthy and temperate.

"Seven years ago, while holding a horse with a rope, the rope got twisted round his thumb and hurt it. The thumb was sore for several days after this, but did not swell. This was in spring; during the summer it felt stiff, and in the following winter the first phalanx swelled up from what was considered to be rheumatism. During the following winter it was at times painful and swollen. The swelling was red, and the veins over it were distended. It came and went more frequently, and seemed to be worse on exposure to cold. It soon continued to be painful even when there was no swelling. This intermittent swelling continued for four years, when he noticed a small lump attached to the outer side of the first phalanx. The lump was bluish and soft; it was very painful, and he thought it was going to form matter. It, however, continued to grow without coming to a head. Eighteen months ago it was opened, and only blood came out; and last August it was opened again, with the same result. The thumb (Fig. 11) was amputated, and the patient shortly afterwards went home. Two years after the amputation, a small nodule appeared in the stump. This was removed by a local practitioner. After that no further recurrence took place, and the patient was reported well in 1906."

After section, the tumour was found to have originated in the front of the first phalanx, and to have expanded the bone for a short distance laterally, but there was no shell of the bone over the main piece of the tumour (Fig. 10). The joints at each end of the phalanx were not affected. The tumour mass was of firm consistence, except towards the margins, where it was soft and reddish, hæmorrhage having taken place into the tissue at these parts. The main mass of the tumour presented a gelatinous appearance, with a network of dense white material, apparently cartilage of firmer consistence than the rest, and with calcareous nodules interspersed.

Microscopic examination showed it to be chondroma, with a relatively large proportion of cells to intercellular substance, the latter being largely fibrous in character, and showing also in some places myxomatous degeneration (Fig. 12).

(6) *Enormous Cartilaginous Tumour of Costal Cartilages and Sternum. Eight years' growth. Death from intrathoracic pressure and sapping of strength.*

The specimen from which the photographs (Figs. 13, 14) were taken, is in the Anatomical Museum of the University of Edinburgh (Os. D. p. 3).

The following is taken from Sir William Turner's account of the specimen in *St. Bartholomew's Hospital Reports*, vol. vi. p. 119 :—

"Thomas E., æt. 62, farm labourer. Eight years ago, when lifting a grain-bag from a cart, 'strained his chest,' came home, and complained to his wife. He went to work again next day, and in the course of a week noticed a lump a little below the middle of his breast-bone, about the size of his thumb-nail. This lump, which was smooth and did not give pain, gradually increased in size. He consulted Dr. W. Jackson, of Bolton-le-Sands, with reference to it, about eighteen months or two years before his death, and on examination the swelling was diagnosed as 'an osteosarcomatous tumour of great dimensions with nodulated surface.' About a month before death, Dr. Jackson found the patient not much emaciated, respiration shallow and rapid; pulse quick and very weak. Heart sounds heard through the tumour; healthy but weak. On the front of the chest was the immense tumour, forming a huge swelling extending from the top of the sternum to below the ensiform cartilage, reaching laterally on the right to the rib-end of the costal cartilages. On the left of the axilla above, and external ends of the costal cartilages below; long diameter, 12 inches; transverse, 9 inches; circumference, 29 inches; antero-posterior diameter on the right side, 6½ inches; on the left, 7 inches. This diameter had an ovoid shape, with the larger end below. It was irregularly nodulated, the depressions and elevations being very slight. The skin stretched over it had a bluish tint. By forcibly elevating it, the fingers could be passed between the tumour and the ribs as far as the border of the sternum on both sides, and there could be no doubt that it sprung from the costal cartilages, and that it was an enchondromatous or osteosarcomatous tumour. The man had very little cough, and up to the time of his death he had expectorated blood but once, and that a very slight streak. He died slowly, May 16, 1870, of debility.

"*Post-Mortem Examination.*—Skin over tumour very thin, pectoral muscles thin, with the fasciculæ separated from each other through extreme stretching and attenuation. On cutting through the ribs, the tumour (Fig. 13) was found to extend into the left chest, filling up the space usually occupied by the left lung and heart; the lung was pressed against the posterior boundary of the chest, and apparently disorganized; the heart was dislocated to the right of the sternum, healthy in structure, though pale. . . . There was no opportunity for examining the state of the other organs."

"The tumour weighed 12 pounds avoirdupois, and was invested by a capsule. It had the characteristic lobular structure, firm texture, and bluish-white semi-translucent appearance of a cartilaginous tumour. Numerous calcareous nodules were scattered over the surface and within the substance of the tumour; several cysts were seen in the intrathoracic part.

"*Microscopic Examination*" (Fig. 14).—"Pearly-white lobules had the characteristic structure of hyaline cartilage, with the cells irregularly arranged in a matrix. . . . The tumour presented, therefore, in various parts of its substance examples of the modes of degeneration to which cartilaginous tumours are liable; the calcareous degeneration ranging from earthy granules, so minute as to be visible only with the microscope, to large irregular nodules; the fatty degeneration from a few scattered globules to the stage in which cells, nuclei, and matrix are so obscured by the

accumulation of refracting particles as to be no longer recognizable; lastly, the cystic change in which cysts with well-formed lining membranes were present."

In this case, the tumour caused the patient's death partly by its growth towards the interior of the chest, and partly by its steady increase in size, thus sapping the patient's strength. This is a tumour, therefore, which deserves to be called locally malignant.

(7) *Enormous Chondrosarcoma of Innominate Bone, following an injury seven years before death. Growth slow at first; very rapid afterwards. Death from sapping of strength.*

The specimen from which the photographs (Figs. 15, 16) were taken was presented to the Museum of the University of Edinburgh (Os. D. p. 61), in February 1868, by Dr. T. Dobson, of Windermere, who sent the following clinical account of the case (*Journal of Anatomy and Physiology*, vol. ii., 1868):—

> "Prior to a fall in the year 1861, in which the man was considerably bruised in the lumbar region, he had enjoyed excellent health. A few months after the fall, he began to walk lame, and complained of pain in the muscles in front of the left thigh. As time went on, these symptoms increased, and in 1865 I detected a tumour about the size of a hen's egg, hard, firm, immovable, with a slightly irregular surface, situated deeply in the left hypogastric region, and apparently springing from the sacro-iliac synchondrosis. It never pulsated nor was influenced by the state of the bowels. As it steadily increased in size, œdema of the left lower limb came on, and the pain increased in severity. . . . The tumour gradually extended upwards, displacing the six lower left ribs upwards and outwards, extending into the right inguinal region, and, by pressure on the veins, occasioned œdema of the right thigh; and the abdominal walls were so thinned that the irregular surface of the tumour was visible to the eye. He died on the 24th of February, worn out with pain and bedsores. It is remarkable that during the whole illness the functions of the bowels and bladder were but little interfered with. Post mortem made twenty hours after death. . . . When the abdomen was opened, the tumour was seen to occupy the whole cavity, except the right hypochondrium and a small portion of the right lumbar region, which contained the stomach, ascending and transverse parts of the colon and small intestines in front, and the liver behind. . . . The weight of the tumour and connected bones was forty-six pounds; the probable weight of the tumour alone, forty-four pounds."

Professor Turner described the characters of the tumour shortly after it had been removed from the body.

" . . . Irregularly and broadly ovoid in form, the narrower end being directed upwards, whilst the broader end was connected with the left innominate bone (Fig. 15). . . . Its longitudinal circumference was three feet six inches. Its greatest transverse circumference, three feet five inches. It was deeply and irregularly lobed. . . . A well-marked fibrous capsule invested the tumour, not only where the serous covering was deficient, but beneath that membrane also. When bisected in the mesial plane of its long axis, the surface of section, which measured eighteen inches by sixteen inches, presented the following appearance: Each of the large irregular lobes

was subdivided into numerous lobules, varying in size from a pea to a walnut, which were invested by thin capsules of connective tissue, continuous with the general fibrous capsule of the entire tumour. Some of the lobules had a pearly lustre and a fine opaque, and almost cartilaginous consistence; others, again, had a pinkish, yellowish, or faint greenish colour. These had a consistency more like that of stiff jelly, and could be enucleated from their capsules with great ease. Though the tumour was firm, and the lobules generally were opaque, yet it had none of the toughness of a fibrous tumour, and could without difficulty be broken down by the fingers. It was succulent, and a yellowish, non-creamy fluid, in which minute oil globules floated, drained away. When the tumour was bisected, several cysts were opened into, of which one was large enough to contain a fœtal head, and from their anterior a turbid yellowish fluid escaped. A smooth, semi-opaque membrane partially lined these cysts; but in part, irregular villous masses projected from the inner wall into the cavity, traversing it much in the same manner as the bands one sees passing across a large vomica in a tuberculous lung. . . . Portions of bone also lay in the anterior tumour detached from the general substance of the ilium.

"*Microscopic Characters*" (Fig. 17).—"These sections of the pearly-white lobules, examined under water with a magnifying power of 200 diameters, were seen to be composed of exquisitely pellucid round, oval, or somewhat flattened cells (*a*), which possessed a very delicate outline, and usually contained a single round or oval nucleus with no trace of granular matter within the cells, or of intercellular substance between them. These cells closely resemble in form those of which the rod of embryonic cartilage, called chorda-dorsalis, is composed, and with some modifications to be next described, these simple cell forms made up the lobules of this enormous tumour. In those lobules which had a yellow colour, whilst the fundamental type of structure was preserved, numerous fat granules, partly free, partly within the cells (*e*), partly within the nuclei, were seen, and this fatty character was especially visible in those lobules which lay next the inner wall of cysts, and evidently pointed to a degeneration of the cells and lobules, preceding probably the cyst formation. . . . Several nuclei also were often seen in a single cell, and not infrequently they exhibited elongations and constructions as if in the process of dividing. . . . It is important to note that the tumour possessed comparatively slight vascularity, and such vessels as it contained were situated in the general fibrous capsule or the prolongations which passed between the lobules, and not amidst the proper cell structure, which, like the cells of the chorda dorsalis, were extravascular. The larger lobules had, however, processes of connective tissue passing into their substances from their investing capsules, which were in many cases so delicate as to be recognized by the microscope, and which served to subdivide their constituent cells into still smaller groups.

"*Classification*. . . . If we accept, therefore, the anatomical classification of tumours, based on their resemblance to normal structure, it should be referred to a group of tumours, having for its type the cells of the rod of embryonic cartilage around which the bodies of the vertebral and the basi-cranial axis are developed."

This tumour caused death mainly, if not entirely, by its enormous growth. It therefore deserves the title of local malignancy even more than the preceding one. Its minute structure in many places is identical with that of rapidly growing hyaline cartilage (Figs. 16, 17).

(8) *Chondrosarcoma of Humerus, following an injury. Enormous growth in nine months; death from exhaustion and hæmorrhage.*

The specimen from which the photographs (Figs. 20, 21) were taken is in the Museum of the R.C.S.Ed. (6. 370).

The following history of the case is taken from John Bell's *Principles of Surgery*, vol. iii. Part I. p. 82:—

> "Alexander Macdonald, a Highlander, from Fort-Augustus—a tall and handsome lad, passing six feet in height, and uncommonly athletic—was put to the Perth Academy for his education in writing, bookkeeping, and such other parts of learning as might qualify him for a counting-house. It was intended to send him to America, a clerk to the North-West Company in the fur trade. In running violently at tennis, in the Academy green, he fell and hurt his shoulder. It was such a bruise as often happens from a fall, without entailing the slightest ill consequence beyond the first pain and swelling; the skin was blackened by the bruise and the joint was sprained; he had excessive pains along the whole arm for twenty-four hours; but it vanished gradually. He imagined himself well; he had recovered everything but the strength of his arm; but after the violence of the pain (which lasted no more than twenty-four hours) was gone, such weakness remained, that though from his great strength he could lift perpendicularly such weights as others could not move, yet he could never raise his arm to his head.
>
> "I was at pains to question his father, a respectable old man, concerning the part which received the injury, and he clearly and decidedly affirmed that it was not the shoulder-joint, but the middle of the bone of the arm, that received the shock. It was along the whole of the arm that he felt the pain, and could distinguish the marks of the bruise. The pain had, after its first violence, totally ceased, as if the part had sustained no permanent injury, and he believed himself well. It was exactly at the end of a month that the pain returned and fixed in the joint, with a very distressing sense of weakness, so that he could not at all raise his arm; if he meant to put on his hat with it, he had to raise it with the other hand, and when thus raised, if he lowered it again without support, the moment it fell unsupported below the level, it descended like lead. Still, he could lift perpendicularly a very great weight; but from this second period of pain we must date the disease. The whole arm swelled, but specially about the shoulder. His cries and shrieks were wild and melancholy. Living in a remote part of the Highlands, it is natural for the father to express himself in the following words, which he invariably uses when I question him in regard to the degree of pain: 'Sir, there was no hour of the night nor day in which you could not hear his wild cries miles off.' He represented the particular pain by saying it seemed as if he had been bored with hot irons; and his cries were so unceasing, as well as so piercing, that 'though they lived in a very long house, they had no sleep from this time forward.'
>
> "That such had been his condition no one could doubt who saw him before his death, for the swelling kept equal pace with these dreadful sufferings. At first the arm seemed chiefly to swell from the shoulder-joint; gradually the

whole arm swelled, and the forearm and hand dwindled. His body, before lusty and strong, was wasted with the agony and want of rest. Yet even at this time, when the arm was monstrously swelled, and before it was entirely oppressed, or the forearm wasted, he could lift as heavy a weight with the left arm as with the right, and even to the last stage, that in which I saw him, his hand was strong to grasp. In the first four months the upper part of the arm had so increased in size that the prominent part exceeded the size of his head, but now, at the end of nine months, it greatly exceeds in size his emaciated body.

"When I went to receive this poor lad, I found him lying deep in the hold of a small sloop, in which he had been transported from Inverness, laid on a coarse mattress, and bolstered up against the shelving side of the vessel; and when the clothes were lifted I solemnly declare that I hardly knew at first what it was that I saw — which was the tumor and which his body, or how to connect in imagination the one with the other. He lay in an inclined and irregular posture, extremely languid, and hardly able to articulate, his head inclining to one side. The tumor, when first exposed by lifting the cloaths, might be mistaken for his body in respect of size, it was of a suitable bulk, and when the lean, yellow, emaciated thorax was next exposed, the tumour seemed so much to exceed it in size, with a shining surface and brilliant colour, that at first I was more confounded than shocked, so impossible was it in the first moments to consider of it as a tumour, or to see its relation to the arm. The forearm was dwindled and shrunk, and projected from the tumour at a strange and unnatural distance from the shoulder. The veins were swelled, like those of a horse's belly; large fungous tumours, as big as oranges, projected in a group from the outside of the arm at the place where, about two months before, a large abscess had burst; and such was the fœtor of the matter running from under these fungi and the langour of this poor emaciated creature, that I had no thought for the present but how to get him conveyed alive to town. After a few days, when he was somewhat recovered from the fatigues of the voyage, I proceeded to write down the history, and examine the actual state of this tumor. I found it throughout solid, consisting chiefly of bone, little cartilaginous, hardly in any part elastic or yielding, and discharging matter, not from any superficial abscess, but apparently from the centre of this enormous mass. I had every reason to believe that the bone and the joint, which certainly were neither broken nor dislocated, had been generally injured, not merely by the shock but by the bruise; that the parts nearest the bone, and connected with it by the periosteum, had been bruised and inflamed; that the extreme pain for the first twenty-four hours indicated only the violence of the immediate injury, but the slow vascular action which succeeded at the distance of a month, proved how deeply the circulation of the bone was affected, and caused that osseous secretion which generated this prodigious shell of bone, while the shaft of the shoulder-bone, from the periosteum of which this callus had been secreted, was in part destroyed by an ulcerating process within. That the ulceration, deep-seated, not only in the bone but in the joint, occasioned those excruciating tortures which were announced by wild and desperate cries night and day; that the matter, bursting at last through every obstacle, had made its way through that ulcerated part of the surface which is studded with the fungous excrescences represented in the drawing (Figs. 18, 19).

"This bursting out of the matter brought relief from the pain, and he now lay in a state of extreme langour, moaning and slumbering. You found it

painful even to question him, he was so feeble; he fell, after a few broken answers, into a slumber of mere debility, and closed his eyes as exhausted; and while I took the sketch of his posture, and of the proportions of this prodigious tumour, he slumbered continually. His extreme weakness precluded every practical experiment, and left for our discussion the speculative question only: 'In a case so deplorable and hopeless, what should we have done at an earlier stage, when the patient's strength was more entire, and youth and vigour (for he was but 21 years of age) on his side?'

"He died in the Royal Infirmary of hæmorrhage, about three weeks after his admission, and these are the notes of the dissection.

"*Dissection*—July 13, 1806.—Having divided the integuments, which were extremely thin, we found on attempting to cleanse the tumour, from one extremity to the other, that it was of a substance much resembling callus; in many places it was so firm and solid, that, after trying in vain to divide it with a strong knife, we were obliged to betake ourselves to the common amputation saw.

"The cells of this bony tumour were everywhere filled with a matter resembling thick cheese; the tumour itself, from its great size and the entire appearance of the os humeri, seemed only to be attached to that bone; but, upon a more minute examination, was plainly a production from its substance. The shoulder-bone could be traced through the whole tumour; but enlarged, spongy, and ulcerated. The upper part of the scapula, the acromion process, and the outer end of the clavicle, could during life be plainly distinguished to be enlarged, and to form part of the tumour; and upon dissection, all the bones forming the shoulder-joint were found to be deeply diseased. The upper and most bulky part of the tumour seemed to proceed as much from these as from the os humeri, and the joint was completely anchylosed."

This portion of the tumour is evidently cartilaginous. The nodules in most places are distinct, but over extensive areas they have been softened and broken down. Calcareous deposits are scattered throughout the substance. John Bell's description of the tumour does not correspond exactly to that of a cartilaginous tumour, when he speaks of matter "resembling thick cheese," unless he means "of the consistence of thick cheese." The reference to this specimen, however, which is given in Sir Charles Bell's Catalogue (the brother of John Bell), makes it clear that this formed a portion at least of the tumour to which John Bell's graphic account, just quoted, refers. The clinical history as to pain and rapid growth bears a very striking resemblance to Dr. Watson's case of chondrosarcoma. (See 10.)

This may be considered to be an extreme case of local malignancy. Whether there were any secondary deposits or not cannot be told, as the post-mortem examination seems to have been confined to the immediate neighbourhood of the tumour.

The microscopic structure of the firm part selected for examination (Fig. 21) is like that of an innocent tumour. The more rapidly growing, and therefore softer, parts have probably disappeared owing to imperfect preservation of the specimen.

(9) *Chondrosarcoma of upper end of Humerus. Rapid local return twice after apparently free removal; cured after third operation.*

The specimen from which the photographs (Figs. 22, 23) were taken is in the Museum of Mr. J. Hodsdon, who obtained it from the late Mr. J. Duncan.

The history attached to the specimen is that the tumour returned after removal, and eventually the scapula and upper limb were removed also. The following account of the case is taken from Professor Syme's monograph *On Excision of the Scapula* (p. 30):—

"On the 23rd of August 1862, Mr. K., a gentleman about 40 years of age, from Manchester, applied to me on account of a painful swelling in his left shoulder. It lay under the deltoid, which was nearly uniformly distended by a firm mass apparently originating from the bone, and enlarging its head to about twice the natural size. The patient stated that in 1860 he had over-exerted his arm by carrying a heavy weight, and in consequence of doing so was for more than a month hardly able to raise it; that in September 1861 he began to feel an acute pain at one particular part of the shoulder, which increased gradually, until the following spring when it became seriously distressing; that he went to Buxton in June or July, without obtaining relief for what was supposed to be rheumatism; that in August he went to London, and consulted two surgeons of eminence, who do not appear to have entertained, or at least expressed, any decided opinions on the subject; and he had therefore come to me.

"I felt no hesitation in stating my belief that the symptoms proceeded from a morbid growth of the bone, and did not admit of remedy except by removal of the part affected; but, to avoid any risk of unnecessary interference from the disease being merely periosteal, advised the application of one or two blisters and small doses of the iodide of potassium. On the 16th of September, finding that there had been no improvement under this treatment, I proceeded to cut out the head of the humerus, as in the case last related, with the effect of removing a fibrocartilaginous growth not affecting the joint, but extending round the bone, and presenting an irregularly tuberculated or nodulated surface. The patient suffered no local or constitutional disturbance from the operation, and on the day three weeks from the time of its performance was able to take a drive.

"The arm soon became strong and serviceable, so that the recovery was deemed complete and permanent. But, early in January 1863, a tumour was felt under the cicatrix, and suggested another visit to me.

"Finding the new growth, which was about the size of a large walnut, quite movable and unconnected with the bone, I at once removed it, and found a thick fibrocartilaginous cyst, with serous contents. The wound quickly healed, and we again hoped that the disease was eradicated. But very soon afterwards I was sorry to hear that a more formidable attack was threatened in the scapular region, where a large growth had become rapidly developed, extending into the axilla, and overlapping the end of the humerus. The opinion of Mr. Paget was then taken, and, being strongly favourable to another attempt, I agreed to undertake it; but as the patient naturally felt averse to another long journey under such distressing circumstances, he requested me to perform the operation at Manchester; which I accordingly did on the 7th of May, assisted by Messrs. Smith and Beever of that city, and Mr. Annandale, who accompanied me.

"As the arm, unfortunately, could not be preserved, instead of cutting in a crucial form I made two semilunar incisions from the acromion process downwards, one on each side of the joint, and terminating at the lower angle of the

scapula. . . . The tumour, which presented precisely the same characters as those of the former growths, adhered inseparably to the glenoid cavity, neck of the scapula, and acromion process; thus rendering any less decided measure than the one adopted inadequate for the purpose.

"Everything went on satisfactorily after the operation. . . . The patient, the last time I heard from him, had been following the hounds."

This tumour exhibited what may be called local dissemination. There is nothing in the microscopic section (Fig. 23) which differs in any important particular from that of the innocent cartilaginous tumours at the beginning of the series.

(10) *Chondrosarcoma of Scapula and Chondromata of Fingers and of Humerus. Rapid growth of Scapular Tumour; successful removal; death from metastases in the lungs.*

The specimens from which the photographs (Figs. 24, 25, 26, 27) were taken were presented to the Museum of the R.C.S.Ed., by Sir Patrick Heron Watson. (6. 367; 6. 369).

"The patient was a gentleman, aged 33. From infancy the joints of both arms were noted as 'peculiar.' The shoulder, elbow, and finger-joints of his right arm were supposed to have been 'put out' by some injury, of which, however, no history was obtainable from his mother. During childhood and boyhood the finger-joints steadily became more 'peculiar,' enlarging gradually till, when he was 18 years of age, the growths formed a decided inconvenience, particularly those on the right hand, all the fingers of which were affected. On the left hand, the middle, ring, and little fingers only had growths. As the tumour of the right middle finger hindered him from writing, the finger was removed by Professor Syme. The patient was at this time fully engaged in hard office work. In 1870, when about 20 years of age, he went to Southern India, and remained there for thirteen years, enjoying, until the growth of the great tumour, perfect health. He was able to write, ride, and play lawn tennis. The growths on his fingers had meanwhile only slightly increased up to about January 1883 (the year of the operation). He then began to feel pain in the right shoulder, and was treated for neuralgia. The pain got worse; the shoulder began to swell; his clothes required altering, and finally he had to keep his arm in a sling outside of his clothes altogether. The pain centred over the bicipital groove, and was very much aggravated by the least pressure.

"By April 1883 he had gradually become invalided, the pain getting steadily worse. He walked with difficulty, till in July he was forced to lie up. After a month in bed he could only stand with help. In August he was carried to Madras for further advice. At this time he could straighten his legs, but the growth was increasing rapidly. At Madras he was advised to return home, and did so, being carried into his bunk in October, and never leaving it during a voyage of thirty days. Being a tall man, his legs were kept permanently bent up, thus acquiring the position described in 'present condition.' On arriving in Edinburgh, he saw Dr. Gillespie. Dr. Patrick Heron Watson was shortly afterwards called in consultation, but thought that any operation was inadvisable, because the patient's general health was in such an unsatisfactory condition.

"By the 17th of December his general condition and blood had considerably improved under treatment, and Dr. Watson decided to remove the arm, scapula, and outer third of the clavicle, along with the tumour, as the only possible means of affording relief to the patient's intense sufferings. He was in a state of constant acute suffering, and could not retain the arm for five minutes in one position. The pain prevented the possibility of sleep for more than three minutes at a time, and he had not slept an hour for many weeks. He had quite a cachectic appearance.

"At this time the tumour of the right scapula rose as a great hump above the line of his shoulder. It was incorporated with the scapula and adjacent parts. It was firm in consistence in some places, and soft and almost fluctuating in others. There were also multiple growths, like small apples, and firm in consistence, on the metacarpal and phalangeal bones of both hands.

"The knees were rigidly semi-flexed, and the patient had scarcely any power over his lower limbs, the muscles of which were much atrophied. The thighs and calves felt brawny.

"Dr. Watson operated on the 17th of December 1883, and the wound healed without a bad symptom.

"Although he made a capital recovery as to wound, he only slowly recovered the use of his legs by the use of rubbing, the 'battery,' and extension at night to straighten the knees. On the 6th of April 1884 his general health was good, but as he was still unable to use his legs, much the same treatment was continued. On the 20th of June 1884 a photograph of the cicatrix was taken. He could then walk with help, and his health was good. During July and August he walked fairly well, and went to the country. In September, on his return, he did not look so well, his colour being dusky. In November 1884 Dr. Burn Murdoch was called to attend him for pains in his chest, on the right side, with shortness of breath and cough. Some pleuritic rubbing was heard, and a copious effusion into both right and left pleural cavities was detected. He died shortly afterwards, in November 1884, from obstruction to respiration and increasing weakness.

"*Autopsy.*—The chest (both sides) was full of fluid, and both lungs were studded over with hard and semi-hard nodular masses. One or two nodules of a similar nature were found on the internal surface of the ribs. (Permission had been given to examine the chest only.)"

The fingers are disfigured by numerous simple cartilaginous tumours of the usual character (Fig. 24). A section of one has been made to show its structure. The firm lobulated cartilaginous substance, interspersed with calcareous and osseous nodules, is characteristic of the slow-growing simple chondroma. A somewhat similar tumour can be seen growing from the outer condyle of the humerus, as well as from the adjacent portions of the bone. The tumour on the scapula has been sliced in one or two places to show its character. It is formed of large masses, surrounded by fibrous tissue. The interior of these masses is broken up into small portions, apparently by the softening of the matrix, so that the tumour has an irregular, honeycombed appearance, which is a great contrast to the firm texture of the chondroma of the fingers, placed in juxtaposition to it. Microscopically (Fig. 25), this tumour consists of a substance resembling embryonic cartilage, showing numerous spindle cells, with a relatively small proportion of its intercellular substance.

Portion of Lung from this Case (Fig. 26).—Nodules of chondrosarcoma are scattered through the lung substance. The nodules on section show a naked-eye appearance similar to that seen in the large tumour of the scapula. Microscopically also, the structure is similar to that of the original tumour, only more definitely embryonic in character (Fig. 27).

II.—Second Gradation Series: Bony and Fibrous Tumours.

It is difficult to obtain for the purpose of illustration osseous tumours of undoubtedly innocent character. Such tumours are, of course, common enough, but they are not preserved so frequently as others which are of more clinical importance. Moreover, when these tumours are presented to a museum, their clinical history is seldom given along with them, perhaps because their mere appearance is considered a sufficient proof of their innocent character. The following illustration is taken from Mr. Oliver Pemberton's *Clinical Illustrations of Various Forms of Cancer.* The patient from whom it was removed after death was the subject of malignant disease of the face.

(1) *Large Osseous Tumour of Femur, quiescent for many years before death, which was due to cancer of the face.*

"J. T., æt. 53, married, by trade an engineer, a spare, tolerably healthy-looking man, was admitted under my care in the hospital on the 20th of April 1857, on account of a large bony tumour of the right thigh, accompanied by the presence of many others of smaller size, situated in various parts of the body, and also because of the appearance of an ulceration of the face.

"*History.*—He states that all the tumours have existed from the date of his birth. Up to the age of 23 there was an increase, more or less marked, in all of them. During their growth he suffered pain and numbness in the limbs where they were chiefly placed, but after their limits appeared to be determined all pain from them ceased. . . .

"*Present State.*—The right thigh is occupied in its lower and middle thirds by a vast tumour which springs from the femur itself, mainly on its posterior aspect. It is somewhat oval in shape—smooth and flattened in front, nodulated at the sides and behind. It is without pain, evidently bony in its nature, with the skin unaltered beyond a little thinning. The soft parts of the popliteal space pass to its outer side, by stretching over it. The movements of the knee-joint are limited by its proximity. The tumour, from above downwards, measures twelve inches, its circumference reaching twenty-seven inches. On the same limb are two other bony tumours, nearly symmetrical in shape, and as large as a good-sized orange; they grow respectively from the inner tuberosity of the tibia and the head of the fibula.

"On the right humerus, just below the insertion of the pectoralis major, is a small conical tumour, about as large as a filbert. This gave him intense pain during its growth. Similar formations, varying in size from a pea to a walnut, are situated on the lower end of the right ulna. On the seventh rib on either side, just external to its cartilage—on the left tibia and fibula, in situations almost exactly corresponding to those on the right, and also on the internal malleolus.

"The sore on the face gradually extended in spite of repeated applications of chloride of zinc, and the patient died exhausted on the 17th of August 1859. The bone tumours had not undergone any change since he had first come under observation. . . ."

"The main tumour attached to the femur (Fig. 28) afforded a well-marked specimen of nodular exostosis, a thin layer of compact bone being everywhere spread over its uneven surface, while its interior was occupied by spongy tissue."

(2) *Osseous Tumour of the Shoulder, of over fifty years' standing. Growth, rapid at first, afterwards inappreciable; death from renal disease.*

The account of this case was published by Dr. A. J. Whiting in the *British Medical Journal*, 1905, vol. i. p. 19. The specimens from which the photographs (Figs. 30, 31) were taken are in the Museum of the Tottenham Hospital, London.

"E. K., a man, æt. 63, was admitted to the Laseron Ward of the Tottenham Hospital on the 10th of March 1904, for chronic Bright's disease.

"*History.*—Between the ages of 12 and 13 the patient injured his left shoulder. Shortly after the accident the shoulder began to enlarge, and it continued to gradually enlarge for about four years. He was then in St. Mary's Hospital, and total amputation of the limb was advised. This he refused. Patient had small-pox at the age of 16, and typhoid fever at the age of 17. Syphilitic infection was denied. He had been a very heavy drinker all his life. Dropsy of the legs was first noticed thirteen years ago. He suffered from this at intervals up to the time of his admission, and for the previous seven weeks he had been getting weaker and very breathless.

"*Family History.*—His mother and one brother died of apoplexy in middle life. Patient was the father of four healthy children. There was no history of malignant disease in the family.

"*State on Admission.*—Patient was very anæmic, cachectic, and of a yellowish complexion. There was no actual jaundice. The tongue was thickly furred and tremulous. His temperature was subnormal throughout.

"*The Tumour.*—The upper end of the left humerus was enormously enlarged, the enlargement being bony, and of equal hardness throughout. No egg-shell crackling could be obtained. The humerus was ankylosed to the scapula by the growth, which extended from its head to the junction of the middle and lower thirds of the shaft. The skin was stretched, but adherent at only one spot, where it had been punctured by a trocar forty-seven years before. The veins over it were enlarged. The elbow was directed outwards, as in a subcoracoid dislocation (Fig. 29). He was able to use his arm fairly well, his occupation being that of a day labourer. There were no pressure symptoms, marked wasting of the muscles, or tingling or numbness of the fingers.

"The patient developed symptoms of uræmic poisoning, and died in a condition of uræmic coma on the 28th of March."

"*Necropsy.*—The muscles of the shoulder-joint affected were slightly wasted. The circumference of the bony tumour was seventeen inches, its length six inches. It extended to within three inches of the elbow-joint. It was found that the growth was firmly ankylosed to the scapula at the glenoid fossa (Fig. 30), but the scapula was not implicated in the tumour

growth. Its surface was uneven, and in a few places it was quite soft, in others quite hard. On applying the saw, the tumour was divided with the greatest ease, in spite of its massive appearance. It was found to be full of spongy, soft bone of the typical asbestos appearance (Fig. 31). In its upper quadrant there was an area about one inch square, consisting of fat.

"The liver and kidneys were contracted and cirrhosed."

"*Remarks by Dr. Whiting.*—The chief interest of this case, and the point which seems to call for its publication, is its bearing on prognosis. That a diagnosis of a malignant tumour should have been given when first he came under observation at St. Mary's Hospital is sufficiently clear from the operation recommended, and the circumstance that for over fifty years he continued to use the condemned limb in his ordinary mechanical duties would hardly even now seem, in the abstract, to justify his refusal. The diagnosis at one time seemed to rest between a simple exostosis and an ossifying sarcoma of a low type of malignancy, but no such alternative was possible after the necropsy. The case is another illustration of the difficulty of distinguishing between different degrees of malignancy in the earlier existence of tumours."

This tumour differs from an ordinary osteoma in its comparatively rapid growth at first, as well as in the large amount of fat which it contained, and in the loose, spongy character of its internal structure. In its *later* history it was innocent in character, but at an earlier period it seems to have been more malignant.

(3) *Very large Osteofibroma of Ulna of eight years' growth. Amputation; no return.*

The specimen from which the photograph (Fig. 32) was taken is in the Surgical Museum of the University of Edinburgh.

The case is described by Professor Spence in the *Monthly Journal of Medical Science*, 1854, vol. xviii., as follows:—

> "I was requested by Dr. Cruickshank, of North Berwick, to visit, with him, Elizabeth Watt, residing at Williamston, who was affected with a large tumour of the forearm.
>
> "About eight years previously she had first observed a small firm swelling a little above the wrist, which continued to increase gradually and slowly, without much pain or inconvenience. About four years prior to my seeing her, she had become alarmed about the tumour, and applied to Dr. Cruickshank, who recognized the disease as osteosarcoma. The swelling at that time was about the size of an egg, limited distinctly to the lower end of the ulna, and had begun to interfere with the motions of the forearm and wrist. Dr. Cruickshank advised her to submit to amputation at the middle of the forearm; but the patient and her friends would not listen to the proposal, and applied for assistance to other practitioners. A variety of remedies, both general and local, seem to have been used, but without any good result. At last she fell into the hands of a bone doctor, and, as far as can be judged from her description of the treatment, he seems to have applied first a strong tincture of iodine, and ultimately some form of escharotic, to the tumour, which gave rise to ulceration at one point, and still more rapid increase of volume, profuse discharge, pain, and great constitutional disturbance. She returned home, the

tumour having attained an enormous size, and her general health completely undermined by the hectic induced by the profuse discharge and pain. Dr. Cruickshank now saw her again, and he found her anxious to submit to any operation to obtain relief.

"At my first visit she was lying in bed, with the enormous solid tumour supported on a pillow. It felt of the consistence of bone, with here and there softer points; the superficial veins were enormously enlarged, the fingers were firmly clenched, and the nails were elongated and curved like claws. A large, deep, ulcerated cavity in the tumour displayed portions of its osseous substance, partly dead and mixed with unhealthy discharge, and emitting a most insupportable fœtor. Her general appearance indicated an extreme degree of debility; she was excessively emaciated, with sunk, anxious features, small, rapid pulse, etc. On examining the axilla, I found decided enlargement of one or two glands.

"The extremely debilitated condition of the patient, together with the enlarged glands in the axilla, and the rapid growth latterly of the tumour, taken in connection with her cachectic look, seemed to militate against amputation; but, on the other hand, the originally simple character of the tumour, its slow progress up to the time of being irritated by stimulating applications, and its still retaining a solid osteosarcomatous appearance, together with the consideration that the mere irritation produced by the ulcerated portion was sufficient to cause enlargement of the axillary glands, and that its removal, though only as a temporary alleviation of her suffering, would be a boon to the patient, made me decide on amputating. Dr. Cruickshank having put the patient under chloroform, I removed the arm by double flap a little below the insertion of the deltoid. There was great venous hæmorrhage in making the incisions, and the blood flowed in a stream from the veins of the tumour, even after the bone was sawn through.

"Six or seven arteries required ligature. After the patient was put in bed she was excessively weak, but gradually revived. An opiate was ordered to be given after the effects of the chloroform passed off.

"Under careful treatment she continued to improve, and was soon able to get up and go out.

"I saw her in September 1853 in excellent health, and examined the stump and axilla carefully. There was not the slightest trace of any tendency to reproduction of the disease, and she still continues in perfect health.

"The tumour, when removed, was found to weigh eight pounds and a half; its length was 14 inches; its greatest circumference, corresponding to about the middle of the forearm, was 18 inches; immediately above the wrist, 16 inches; and near the elbow, 12 inches. It consisted almost entirely of osseous matter, with an admixture of soft fibrocartilaginous-looking deposit. The great vessels and nerves of the forearm, together with the muscles and tendons, passed into and through the tumour, or formed grooves for themselves, more or less deep, as represented in the accompanying plate. The diseased growth seemed limited at each extremity by the articular cartilage; but, although commencing distinctly in the ulna, the disease had progressed laterally so as to blend the shafts of the ulna and radius inseparably into one general mass. Neither the humerus superiorly nor the carpus inferiorly were implicated, but the cartilage of incrustation of the bones of the forearm was partially absorbed. The veins on the surface of the tumour were of enormous size, as seen during its dissection."

In this case the tissues do not seem to have been infiltrated, but the local overgrowth was excessive.

The specimen had been dissected but not macerated, hence the arrangement of the bone-plates is not clearly seen. Still, the mode of preparation enables one to recognize the resemblance in structure between this tumour and the large bony tumours which are placed near it in this gradation series. It resembles them also in its continuous growth.

(4) *Enormous Fibro-osseous Tumour of the Lower Jaw. Growth for about nine years; removal, along with greater part of lower jaw; no return. Excellent health seventeen years afterwards.*

The specimen from which the photographs (Figs. 34, 35) were taken was presented to the Anatomical Museum of the University of Edinburgh by Lord Lister.

The following account is by Professor Syme:—

"Between eight and nine years ago Robert Penman, from Coldstream, then 16 years old, noticed a hard swelling of the gum on the outer side of the grinding teeth of the lower jaw. The swelling was not painful, but gradually increased. When it attained the size of an egg, he applied to a surgeon of the neighbourhood, who extracted three of the adjoining teeth. It then grew more rapidly, and having at length become as large as an orange, induced him to repair to the Royal Infirmary of this city, where it was removed, *i.e.* cut off from the bone. The wound did not heal, and the actual cautery was repeatedly applied in vain to make it do so. After remaining eight months in the Infirmary, he returned home; but finding the tumour rapidly and regularly increasing he, two years afterwards, came again to Edinburgh, and consulted a distinguished operating surgeon (now in London), who declined to make any attempt towards his relief. He went home with the fearful prospect of a certain lingering and painful dissolution; and it was after *three years and a half* spent in this miserable state that Dr. Sibbald of this city happened to see him. Though the tumour was then nearly three times larger than it was when the patient last quitted Edinburgh, Dr. Sibbald felt persuaded that it was still within the reach of surgery, and therefore encouraged the young man to come once more to town, which he accordingly did.

"Though prepared for something very extraordinary, I certainly was astonished at first sight of the patient (Fig. 33).

"The mouth was placed diagonally across the face, and had suffered such a monstrous distension as to measure fifteen inches in circumference. The throat of the patient was almost obliterated in appearance, there being only about two inches of it visible above the sternum, so that the cricoid cartilage of the larynx was on the level with that bone. When the tumour was viewed in profile, it extended eight inches from the front of the neck. It completely filled the mouth, and occupied all the space below it from jaw to jaw. The tongue was thrust out of its place, and lay between the teeth and cheek of the right side. The only portion of the jaw not implicated in the disease, was the right ramus and base of the same side, from the bicuspid teeth backwards. The tumour, where covered by the integuments, was uniformly very firm, and for the most part distinctly osseous. The part which appeared through the mouth was a florid, irregular, fungous-looking mass of firm consistence, from which an alarming hæmorrhage had occasionally occurred; and for the last three or four

weeks there had been almost daily a discharge of blood to the extent of one or two ounces. Notwithstanding the great bulk of the tumour, the patient could move his jaw pretty freely in all directions. With the exception of the disease now described, Penman enjoyed good health. He was a tall, well-made, though much emaciated, intelligent young man, and possessed uncommon fortitude." The tumour, along with more than half the lower jaw, was removed by Mr. Syme on the 7th of July 1828, and the patient made a good recovery.

In 1848 Mr. Syme added the following note:—"About two years ago, and consequently seventeen years after this operation, I was stopped in the street by a well-dressed, respectable-looking man, who introduced himself as Penman. He told me that, after working several years at home as a bootmaker, he had gone in quest of better wages to New York; that he had spent ten years in America, whence he had just arrived; and that he proposed to return there after a short visit to his native country. I was no less surprised than pleased to see how little the operation had injured either his appearance or articulation. Careful inspection, indeed, was required to enable an ordinary observer to detect anything peculiar in either of these respects." (Syme's *Contributions to the Pathology and Practice of Surgery*, 1848, p. 13.)

Fine plates and spicules of bone radiate irregularly outwards from the jaw (Figs. 34, 35). The tumour thus resembles a periosteal sarcoma in structure more than an ordinary osteoma. Yet, unless there had been no dissemination, the operation would not have eradicated the disease as it did.

(5) *Osteosarcoma of Skull, of eight years' growth.*

The specimen from which the photograph (Fig. 36) was taken is in the Museum of the R.C.S.Ed. (6. 400).

"The patient was a herd-girl, æt. 26. About eight years before her death she exhibited symptoms of dementia, which gradually advanced to a maniacal state. She suffered from fearful headaches. A growth appeared on the side of her head, on the right parietal bone, and gradually increased in size. Suppuration took place in it, and opened externally."

"The whole top of the skull is covered with—in fact, is converted into—a very extensive growth of new bone in the form of plates and processes, projecting outwards from the surface. At places, the skull has been penetrated. A limited amount of the new bone formation is seen in the interior."

The structure of this specimen resembles that of an osteosarcoma. Yet the growth was comparatively slow, and the patient would probably have lived longer had the bone involved not been the skull.

(6) *Osteosarcoma of Femur. Spontaneous fracture.*

The specimen from which the photograph (Fig. 37) was taken is in the Anatomical Museum of the University of Edinburgh (Os. D. p. 76). The following is the account given in the Catalogue:—

"The upper two-thirds of a femur, in which the periosteal surface is occupied by a mass of irregular new bone, representing the ossified portion of a sarcoma, which enveloped the shaft in this situation. Spontaneous fracture occurred through the trochanters."

From the description, it would appear that the tumour has been considered to be a sarcoma, probably from its clinical characters, although unfortunately no record of the case, or clue by which it can be traced, has been preserved. An examination of the specimen confirms the view of sarcoma, for we can see where there has been spontaneous fracture, and the irregularity of the surface is much greater than is found in an ordinary osteoma, although the plates of bone are firmer and stronger than those of a typical ossifying sarcoma.

(7) *Osteofibroma of Femur. Gradual increase for six years; local dissemination; amputation; death, three months afterwards, from pulmonary congestion and heart failure.*

The specimen from which the photographs (Figs. 38, 39, 40, 41) were taken was presented by Professor Chiene to the Museum of the R.C.S.Ed. (6. 393).

> "The patient, a woman, æt. 33, was admitted to Professor Chiene's ward in October 1890.
>
> "Five or six years before admission, she thinks she sustained a sprain of the knee, and ever since then the knee has been swollen, getting gradually larger, but never painful. The patient has never been laid up, and only had difficulty in walking for the first time, two months before admission. About that time one lump appeared in the popliteal space, and another over the inner tuberosity of the tibia. These two have grown rapidly, but painlessly—the one over the femur the more slowly. On admission, the patient had no pain in the swellings, and could walk with the aid of a stick. She had some numbness and pain in the toes and foot, and the leg was rather cold. The right knee measured twenty-three inches in circumference at the popliteal space. There were three special swellings; the largest and uppermost, surrounding the lower third of the femur, seemed to grow from the epiphyseal line. The middle one filled up the popliteal space, and the lowest was on the anterior and inner aspect of the leg. These swellings were smooth and rounded; the skin was drawn tightly round them, but not involved."

Dr. Niven, of Newburgh, Fife, in answer to an inquiry as to her subsequent history, reports that, after she returned home from the infirmary in November 1890, she never gained strength, and died on the 21st of January 1891 from congestion of the lung, with heart failure. Her general health had apparently been fairly good before the operation, but she failed rapidly after Christmas 1890. She was not known to have had phthisis. There was no post-mortem examination. It is therefore possible that metastatic deposits in the lung may have been the cause of death; but in the absence of definite knowledge on that point, the tumour may be considered to be semi-malignant.

"After removal by amputation on the 15th of October, the tumour was sawn up, and found to be capsulated, smooth, and lobulated. The lower tumour had a watered-silk appearance, like the section of a fibrous tumour. Two separate nodules of tumour substance were found in the gastrocnemius, and both contained bone. The main mass was found fused with the femur, and was fibrous externally and osseous internally. The popliteal

portion was cartilaginous, and showed a transition between fibrous tissue and cartilage. The tumour was considered an 'osteochondro-fibroma,' as it was composed chiefly of bone, fibrous tissue, and a little cartilage.

"The specimen has been stained on one side with logwood (Fig. 38), which shows the difference between the osseous and the fibrous parts. The cancellated tissue at the lower end of the femur is replaced by condensed bone, like that in the substance of the femur, but the outline of the shaft is still perceptible at places. Some of the new bone forming the tumour is extremely hard and dense."

A portion of the outside of the tumour has been macerated, to show its bony structure.

"The macerated section (Fig. 41) shows the bone to be somewhat porous after the removal of the fibrous tissue. In many places it is composed of plates lying at varying distances from one another, but seldom showing the usual characters of cancellated tissue. The outer surface of the bone (Fig. 40) is rough, in most places owing to the intervals between the plates of bone, but at others, from needle-like radiating processes, resembling those seen in an ossifying sarcoma."

There are several separate pieces of bone shown detached from the main mass.

This tumour may be classed as "simple in the slowness of its growth and high development of most of its tissue, including a large proportion of bone, but as 'malignant' in the steady increase of its size, in having disconnected centres of growth, as well as in the arrangement of its bony plates. It should be stated also that, while most of the fibrous tissue which formed it was fully developed, there were more rapidly growing parts, which were softer in consistence and more embryonic in character."

(8) *Large Osseous Tumour of Femur of five years' growth, removed by amputation through the thigh. Return in stump; second amputation five years after the first; recurrence two years later; death from sloughing and sepsis twenty-five years after the appearance of the tumour.*

The specimens from which the photographs (Figs. 42, 43) were taken are in the Museum of the R.C.S.Eng. In the Catalogue, vol. i. Nos. 1655–1656, they are described as follows:—

1655. "The lower half of a femur and the upper halves of a tibia and fibula, together with a large, elongated, oval osteosarcoma" (Fig. 42). "The tumour is attached to nearly the whole of the posterior and lateral surfaces of the lower third of the femur, and to the ends of the tibia and fibula, so that it surrounds, and has immovably fixed, the knee-joint. Its base is rather constricted, and at the upper part it far overlaps the femur. A part of it also extends from the front into the cavity of the joint, impacted between the heads of the femur and tibia. Like the preceding specimens, the tumour is composed of a hard and heavy, dry, osseous substance, arranged so as to present a coarsely fibrous aspect; and its surface is uneven and fasciculated, bundles of osseous fibres running in various directions on it. It measures ten inches in its extreme length, and nearly three inches in its

greatest thickness. The femur, near the part to which the growth of bone is fixed, appears healthy in its texture, but is rather enlarged. The popliteal artery, vein, and nerve are shown passing over the surface of the growth, and, in one situation, running through it. The posterior tibial and peroneal veins are distended and varicose."

> "The patient was a strong muscular wheelwright, 45 years old. He ascribed the disease to a blow received five years before the limb was removed, while he was in the army. The knee-joint regularly and slowly enlarged, and at last became the seat of severe pain, like that of neuralgia. The leg also became very œdematous. The limb was therefore amputated. In the operation the femoral vein bled profusely and very obstinately; but the patient recovered, and remained well for five years; at the end of which he began to suffer severe attacks of pain in the stump, and an enlargement at the inner side of the remaining part of the femur was felt. These increased, and a second amputation was performed. The femoral vein again bled as much as before; but the patient again recovered speedily from the effects of the operation."

The stump of the femur removed in the second amputation is the next described specimen.

"From the Museum of George Langstaff, Esq."

1656. "The stump of the femur mentioned in the preceding description, with an osteosarcoma formed by its inner side" (Fig. 43). "The stump is quite healthy, and the tumour is not attached to it, but appeared to be intimately connected with the outer surface of the periosteum. The tumour is very irregular in its form, about four inches in length, and three inches in its greatest breadth and thickness. It has the same fibrous and fasciculated appearance, and the same general plan of structure as that in the preceding preparation; the femoral artery runs through its middle.

> "Two years after the second amputation, a similar growth began to form about the stump. It regularly increased, but although sometimes painful, and producing much inconvenience by its increasing size, it did not materially affect the patient's general health, and he was able to pursue his business actively, and was strong and robust for fourteen years after the second amputation. The integuments over the tumour then beginning to inflame and slough, he died, nearly twenty-five years after the commencement of the disease."

The tumour with which he died is shown in the next specimen.[1]

1657. "The mass of osteosarcoma referred to in the preceding history. It is of an irregularly roundish form, and presents the same fasciculated and fibrous appearance on its surface, and the same soft, friable, and crumbling texture, as many of the preceding tumours do. It measures twenty-nine inches in circumference. The remains of the femur are lost in it; and it involves nearly the whole of the os innominatum. Parts of the ischium and ilium may be traced by their external forms; but they are nearly covered with osseous growths, and contain the same kind of morbid osseous structure in their cancellous tissue.

"Presented by William R. Barlow, Esq."

[1] The specimen has now disappeared from the Museum, and cannot be traced.

(9) *Cystic Osteosarcoma of Femur, with the development of numerous bony plates and processes.*

The specimen from which the photograph (Fig. 44) was taken is in the Museum of the R.C.S.Ed. (6. 406).

In this case the tumour is said to have occupied the whole of the thigh from the knee to the hip-joint, and was cystic in places, but we have no other record of its clinical history.

There is a remarkable development of delicate osseous plates growing from the shaft. These plates are themselves composed of finer processes and plates of bone. The open nature of the larger plates may be associated with the cystic character of the tumour.

The tumour has a fairly large development of bone in its structure. The plates of which the bony structure is made up are so well formed that we may consider this to be an example of the slow growing, less malignant form of sarcoma.

(10) *Osteosarcoma of the Tibia of a young person.*

The specimen from which the photograph (Fig. 45) was taken is in the Museum of the R.C.S.Ed. (6. 398).

"A very large osseous tumour has grown from the upper end of the bone. The only recognizable part of the shaft at the upper end is a small portion on the posterior surface. The surface is thrown out into numerous irregular processes of somewhat friable bone, directed outwards from the shaft.

"From the amount of bone formed, this tumour has probably been of comparatively slow growth. Still, the bone is soft and friable, and the character of the bony spicules closely resembles that which is seen in a typical sarcoma."

(11) *Osteosarcoma of the Femur, of nine months' growth. Amputation; recurrence in the stump; death; metastasis in lungs and pleura.*

The specimens from which the photographs (Figs. 46, 47, 48, 49) were taken are in the Pathological Museum of the University of Cambridge. (Sir George Humphrey's Catalogue, 1887, part iii. Nos. 1723–1725.)

> "Amputated by me from a girl, æt. 16, in A. H. Disease commenced nine months previously with pain and swelling. The glands in the groin somewhat enlarged. The disease increased in these glands and in the pelvis, and affected the interior of the thorax, the lungs, and pleura."

The specimen removed by the amputation (Figs. 46, 47) shows no visible affection of the bone at the level of the saw-cut. The appearance, however, of the cut end of the upper portion of the femur, which was removed after death (Figs. 48, 49), indicates that the tumour had probably infected the bone at that point at the time of the amputation.

The new bone is softer and more friable, and the bony plates and spicules less well formed than in the less malignant forms of this disease.

(12) *Osteosarcoma of lower end of Femur.*

The specimen from which the photograph (Fig. 50) was taken is in the Museum of the R.C.S.Ed. (6. 404).

In this specimen there is an extensive formation of new bone round the lower end down to the articular surface, and filling up the intercondyloid notch. The bone is composed of delicate plates and processes, extending outwards from the surface of the shaft, and more or less closely packed together at different places. Above the new growth for some distance, the surface of the bone is rarefied, and beyond that there is a crust of new periosteal bone.

Unfortunately, there is no clinical account of this case; but from the soft character of the new bone, and its arrangement in the form of delicate plates and processes, it may be considered to be a typical example of periosteal sarcoma, of definitely malignant character.

(13) *Periosteal Sarcoma of the lower end of the Femur, with only a small proportion of bone developed.*

The specimen from which the photograph (Fig. 51) was taken is in the Museum of the University of Edinburgh (Os. D. p. 69).

> "The patient was a girl. Professor Spence amputated the limb at the hip-joint."

In this specimen, very little bony tissue has developed. The tumour seems to have grown from the periosteum, and to have consisted chiefly of sarcomatous material.

(14) *Periosteal Sarcoma of the lower end of the Femur, similar to the last. Twelve months' growth; metastatic deposits in brain by that time.*

The specimen from which the photographs (Figs. 52, 53, 54) were taken is in the Museum of the R.C.S.Ed. (6. 409).

> "The patient was an athletic and powerful man, about 35 years of age. For some months before amputation was performed, he had felt obscure pains about the knee. These were thought to be due to varicose veins. Afterwards a swelling appeared, and even then the condition was obscure. He was seen by several leading surgeons, and the diagnosis of sarcoma was at length arrived at. Amputation below the trochanter was performed by Dr. John Duncan, nearly a year after the symptoms first began. The patient made an excellent recovery, and had returned to business, when symptoms of brain disease appeared, and from this, after a few weeks' illness, he died."

"The section (Fig. 52) shows the tumour to be growing round the outside of the bone, which is, however, also partly affected in the interior. The substance of the tumour is vascular, soft, and friable, with only a few bony spicules. Under the microscope it is a large spindle-celled sarcoma."

Photomicrographs are shown of the more fibrous part (Fig. 53), and also of the more cellular part (Fig. 54). It is evident from the clinical *history* that secondary deposits in the brain must have been present at the time of the amputation, which was within a year of the first appearance of symptoms.

(15) *Very Malignant Periosteal Sarcoma of the Shaft of the Femur. Growth in six months; metastasis by that time.*

The specimen and cast from which the photographs (Figs. 55, 56, 57) were taken are in the Museum of the R.C.S.Ed. (6. 418; 6. 419).

"John Wright, æt. 13, was admitted into the Royal Infirmary under Dr. Handyside, on the 13th of June 1843, with an extensive tumour of the left thigh-bone.

"Six years since he had an attack of scarlatina, on recovering from which the left thigh remained weaker than the other, and appeared also to be smaller in size. For this the part had been rubbed frequently with various ointments. He continued to go about, otherwise quite well, till about six months ago, when, during the night, he was suddenly seized with violent pain in the thigh. Poultices were next applied to the affected part, and afterwards sinapisms and a few leeches; but under the treatment the thigh increased rapidly in size. Since then the tumour has gradually increased, and of late he has experienced considerable uneasiness from the frequent pain in it, and the deprivation of sleep thus occasioned.

"On examination, the thigh was found to be much enlarged, especially at its middle, whence it tapered gradually towards each extremity. The tumour was hard and inelastic, connected evidently with the os femoris; and it occupied about the three middle fifths of that bone, leaving its extremities of nearly the normal size. Its surface was smooth and regular, and over it the muscles and other soft parts could be moved freely. The integument over the disease presented a somewhat glistening appearance, but was not discoloured; and beneath it there appeared some faint blue lines, indicating distension of the superficial veins. The tumour was the seat of acute, darting pain, which became increased towards night, and also underwent occasionally severe exacerbations.

"The lymphatic glands of the groin and of the rest of the body were carefully examined, and found not to be enlarged or otherwise affected. The motions of the hip-joint were perfect, and were performed without giving rise to pain. The limb below the knee was much emaciated. The countenance of the patient was sallow and had an emaciated appearance, and his tongue was of a bright red colour. His body generally was not much emaciated, and his health appeared on the whole to be good."—*The London and Edinburgh Monthly Journal of Medical Science.* Report of Case by John Struthers, Esq., House Surgeon, Royal Infirmary, vol. v., 1845.

"On the 13th of June the thigh was amputated at the hip-joint by Dr. Handyside by the transfixion method, and the patient made a good recovery; and six weeks after the operation, *i.e.* the 5th of August, he left the Royal Infirmary, with the ligature still discharging, but the stump otherwise doing well.

"Soon afterwards, he complained of occasional frontal headache, followed by pain in the left orbit and eyeball, with increased sensibility to light and lachrymation. About the middle of August a small chronic abscess formed over the occiput. These pains subsided for a time, but by the end of September had returned with such severity as to confine him to the house. By the end of October Dr. Handyside drew up the following report:—'The left eyeball was very prominent and discoloured; almost complete loss of vision. The eyelids were so much tumefied as almost to conceal the eyeballs, and the veins of the eyelids were very conspicuous, being enlarged and tortuous. The orbit itself appeared to be also enlarged and prominent, especially towards its upper and

outer part, forming there a hard inelastic swelling. These parts were the seat of continual stinging pain, which prevented sleep and was fast undermining his strength. Three chronic abscesses were situated over various parts of the head. There was a tumour of the size of an egg on the left hypochondrium, which was firmly adherent to and connected with the cartilages of the upper false ribs. It was slightly elastic to the feel, had grown rapidly, and was the seat of acute darting pains, being, like the tumour of the orbit, decidedly of a malignant character. The disease seemed to be fairly begun in the stump, particularly in that part of it which had been irritated by the long retention of the ligatures, as, at the part where the last ligature had lain, a small pale-coloured fungus protruded. The patient's body generally was emaciated, and his strength was worn down by the continued pain and the malignant hectic. To procure sleep, he had been for some time in the habit of taking frequent and full doses of the solution of the muriate of morphia.'

"After this he rapidly sank, and died on the 11th of November, four and a half months after the operation. No post-mortem examination could be obtained."

"The tumour is lobulated on the surface, but has infiltrated the muscle, part of which is adherent to it. On the surface of the femur there are indications of erosion at some places, and of development of bone at others. The surface of section shows the femur to have been somewhat condensed in the interior, with tumour substance in the medullary cavity above the condensed part. Below it the cancelli form large spaces, and these at the time of section, also contained sarcomatous material, part of which has since fallen out. The neck of the bone is partially absorbed, and the head is flattened from above. The whole bone was found 'more soft and sectile than natural.'"

In microscopical character (Fig. 57) this specimen resembles the preceding one.

In this case the patient died, with undoubted signs of dissemination, within a year of the first onset. As the amputation was performed about six months after the symptoms were first observed, the cells of the tumour must have been disseminated by that time.

(16) *Periosteal Sarcoma of lower end of Femur. Growth in four months; amputation at hip-joint; death.*

In this case there are only two small portions of the tumour in the Museum of the R.C.S.Ed. (6. 421; 6. 422). From these the photographs (Figs. 58, 59, 60) have been taken.

"R. W., æt. 18. Was admitted to the Royal Infirmary, Edinburgh, on the 4th of September 1888. His mother and an aunt had died of consumption, but his family history was otherwise good.

"The swelling dated from an injury in the beginning of June of the same year. At first there was swelling and pain at the inner side of the knee. These increased rapidly, and in three weeks quite prevented him from walking. The swelling varied in size from time to time, and the pain, which increased with the swelling, was greater at night. It was sometimes sharp, sometimes aching. Blistering was tried without avail. There was difficulty at first in diagnosing between tubercular disease of the knee-joint and sarcoma of the

lower end of the femur. The latter, however, was finally decided upon, and on the 10th of September amputation was performed at the hip-joint. Two days afterwards he died."

"The disease seems to have begun in the periosteum, just above the epiphyseal line, and to have spread in all directions, *i.e.* along the surface of the bone and into the medulla, into the soft textures of the joint, and outwards into the thigh (Fig. 58). The disease has extended higher under the periosteum than it has in the medulla. The specimen was injected first with carmine and gelatine, and afterwards with tallow and vermilion, and the latter injection mass can be seen in numerous medium-sized arteries at the margin of the tumour, and also in many places within its substance."

As there was no post-mortem examination in this case, it is not possible to say whether disseminated nodules were present at the time of his death, or not. The tumour had grown in about three months, and the amount of bone developed was very small. The macerated portion of the tumour (Fig. 59) has the following characters:—

"The surface of the condyle, and of the shaft of the femur for four or five inches above it, is rarefied and partly absorbed. Above that there has been a slight but distinct development of the spicular bone, characteristic of ossifying sarcomata (Fig. 59). This, as it is traced upwards, forms a porous crust, which fades gradually away; but its margin is distinguishable from the surface above, which is that found in periosteal irritation."

The structure of the part, of which there is a microscopic section, is that of embryonic connective tissue (Fig. 60).

III.—Third Gradation Series: Medullary or Central Tumours.

(1) *Large Central Tumour of lower end of Femur; eight years' growth.*

The specimen from which the photographs (Figs. 61, 62) were taken is in the Museum of the R.C.S.Ed. (6. 428).

"The patient, M. G., a young woman æt. 27, a dressmaker, was admitted to the Royal Infirmary, Edinburgh, on the 8th of November 1888, suffering from a large tumour affecting her knee.

"She, though never very strong, had always had fair health until eight years ago, when she fell and hurt her left knee. It was sprained, according to her doctor, and was 'put in' by a bone-setter, after which she could walk. The knee remained swollen, but was not painful. She used a crutch till three years ago. In July 1888 'rheumatism' and swelling all round the knee-joint set in, and this has gradually increased until it has reached its present size. It is not painful.

"The tumour, which is in the neighbourhood of the knee, measures twenty-four inches and a half in circumference, and fifteen inches in length. The patient can walk, but the knee is somewhat flexed.

"The leg was amputated by a postero-internal flap, and the patient did well, except for occasional attacks of gastritis, to which she was previously subject.

"She was discharged cured on the 14th of January 1889."

"The tumour is composed partly of bone, partly of fibrous tissue, and partly of a soft substance, which has been breaking down. The bony part,

consisting of both cancellous and compact tissue, forms walls and septa for the softer portions. The soft tumour substance has apparently grown through the lower end of the femur, and stretched the soft parts beyond it. Part of the cartilaginous surface of the condyle still remains apparently normal. The soft substance is composed of round and spindle cells, with numerous giant cells."

In this case the bone and fibrous tissue can be seen by the naked eye (Fig. 61), while under the microscope the soft material has the so-called "fibroplastic" spindle cells, with numerous large giant cells (Fig. 62).

This tumour may therefore be considered a slowly growing myeloid tumour—with much accompanying bone formation.

(2) *Myeloid Tumour of Lower Jaw, of comparatively rapid growth, but without infiltration or metastatic deposit.*

The specimen from which the photographs (Figs. 63, 64) were taken is in the Museum of the R.C.S.Ed. (6. 484).

"William D., æt. 10, was admitted into the Royal Infirmary, Edinburgh, on the 23rd of July 1890.

"About three months ago patient noticed a small lump growing on his gum. The patient had some bad teeth extracted, which were supposed to have caused the swelling. He thinks it was less for a time, but shortly afterwards it began to enlarge rapidly. Since that time it has remained much the same as it is now.

"Growing from the inferior maxilla, in the position of the two middle and left lateral incisor teeth, a rounded swelling projected into the mouth, dusky red in colour, except at the top, where it was pigmented. It was soft to the touch, and bled easily. After the patient had been in hospital for some time the swelling became firmer. He felt no pain from it, but could not masticate his food properly, and his mouth had a nasty taste and a fœtid odour.

"The general health and family history are good.

"On the 12th of August 1890 the patient was put under chloroform, and Mr. Cathcart freely excised the tumour, with the adjacent bone, and removed one or two enlarged glands below the angle of the jaw.

"In August 1892 the boy was brought to the Infirmary to report himself. There was no return of the tumour, and he was in good health. There was some slight enlargement of the lymphatic glands below the lower jaw, but they were in all probability not connected with the tumour.

"Some years later the boy was seen in excellent health."

"The section of the tumour shows that it has grown out from the centre, and has caused absorption of the greater part of the bone, except along the lower border."

The interest in this case lies in the absence of any local or general dissemination, in spite of the rapid growth and of the appearance of fungation in the mouth. The enlargement of glands noted at the time of operation was considered to be due to sepsis rather than to a secondary deposit. They were removed, however, as a precaution, and were found to be inflammatory in character.

The usual microscopic characteristics of a myeloid tumour are shown in the microphotograph (Fig. 64). The giant cells are large.

(3) *Myeloid Tumour of the lower end of the Humerus. Excision of the affected part of humerus; no return.*

The specimens from which the photographs (Figs. 65, 66) were taken are in Mr. J. Hodsdon's private Museum.

> "The patient was a young woman. Mr. Hodsdon was consulted about a condition of the elbow, which he diagnosed to be a myeloid tumour of the lower end of the humerus. The affected part of the bone was excised. The upper of the three pieces (Fig. 65) was the uppermost slice removed from the humerus, as the tumour had burrowed upwards for some distance above the joint. The patient recovered with a useful joint, and was in perfect health ten years after the operation."

The microscopic characters of a myeloid tumour are well shown in the photomicrograph (Fig. 66). The giant cells are numerous and large.

(4) *Myeloid Tumour of the head of the Tibia; of fourteen months' standing; probably more malignant than preceding specimens.*

The specimen from which the photographs (Figs. 67, 68) were taken is in the Museum of the R.C.S.Ed. (6. 429).

> "C. W., æt. 36, was admitted to Ward 12, Royal Infirmary, Edinburgh, in April 1890, suffering from swelling over the head of the tibia. Fourteen months before, he had received a blow on the leg by a falling stone, which kept him from work for a few days, and caused him pain, but no other discomfort. This was followed by a swelling, which was incised five months later, with negative results. Gradually the swelling increased in size. The patient had been losing flesh for four or five months. On admission, there was a large swelling over the head of the tibia, painful on pressure, and yielding with a crackling sensation. On the 4th of April, Mr. Duncan amputated the leg at the knee-joint, and the patient made a good recovery.
>
> "In most parts the marginal bone has been reduced to a mere shell. Below, and near the outer tuberosity, the tumour substance is invading the healthy-looking bone, but with very little infiltration.
>
> "When fresh, the tumour had the characteristic appearance of a myeloid sarcoma. At one spot, *i.e.* below the crucial ligaments, there was some greyish sarcomatous-looking substance, but all the rest was like blood-clot, crimson, orange, and yellow in colour, as if in varying stages of decolorisation. These appearances are now much altered by the action of the spirit.
>
> "The blow had evidently broken the fibula, and seems to have splintered the tibia."

The microscopic appearances (Fig. 68) of the part selected for examination has a more malignant character than that in the preceding specimens. The giant cells are smaller and fewer, and the other cells are mostly round cells instead of the spindle cells which are generally seen in the innocent forms of this kind of tumour.

(5) *Dried specimen illustrating a comparatively slow growing form of Central Tumour in a child.*

The specimen from which the photograph (Fig. 69) was taken is in the Museum of the R.C.S.Ed. (6. 433).

" The lower half of the tibia has been destroyed by what must have been a central tumour. The affected part is represented merely by a membrane at the back and outer side, continuous above with the shaft. The interior of the remains of the cavity is smooth. The fibula in the region of the tumour has been flattened out into an elongated plate, and is blended with the membranous wall of the cavity. Apparently, therefore, the tumour has been of comparatively slow growth. The bones of the foot are light and translucent."

(6) *Rapidly growing Myeloid Tumour of the lower end of the Femur.*

The specimen from which the photographs (Figs. 70, 71) were taken is in the Museum of the R.C.S.Ed. (6. 437).

" A large tumour growing from the lower end of the femur has almost entirely replaced it. The tumour is composed of lobules of soft substance, separated by firmer and more vascular tissue, and breaking down in the centre. The tumour has invaded the knee-joint, and has grown through the femur all round, especially behind. The bone is eroded but not expanded, and is not apparently infiltrated. A distinct capsule has been formed by the soft parts round the tumour."

This tumour has apparently grown too rapidly to allow of a capsule being formed of bone, but yet sufficiently slowly to allow of a capsule being formed by the soft parts.

Microscopic examination (Fig. 71) shows that the giant cells are relatively few and small, while the other cells present are mostly round.

(7) *Rapidly growing and fungating Myeloid Tumour of the lower end of the Humerus.*

The specimen and cast from which the photographs (Figs. 72, 73, 74) were taken are in the Museum of the R.C.S.Ed. (6. 435; 6. 436).

View taken from a cast (Fig. 72) and from a section of the specimen itself (Fig. 73). In this case the growth has apparently taken place so rapidly that the bone has been for the most part absorbed, and the tumour has broken through the soft parts and fungated on the surface. In the part selected for microscopic examination (Fig. 74), the giant cells are relatively few and small, with a large proportion of spindle cells.

(8) *Rapidly growing and fungating Myeloid Tumour of the Tibia.*

The specimen from which the photographs (Figs. 75, 76, 77) were taken is in Mr. Hodsdon's Private Museum.

The lower end of the tibia has been broken up and destroyed by the growth of the tumour without any signs of expansion (Fig. 75). Externally, there is a large fungating and sloughy-looking mass.

Under the microscope, the firmer parts show a considerable proportion of giant cells, with a good many round and a few spindle cells (Fig. 76). In the fungating portion of the tumour a considerable number of giant cells can be seen, but the proper structure of the tumour is concealed by extravasated blood (Fig. 77).

This tumour shows the characters of local malignancy, but as the

clinical history of the specimen is not known, it is not possible to say whether other features of malignancy were present or not.

As I have not been able to find a specimen of myeloid tumour which had undoubted malignant characters in any of the Museums in Edinburgh, I must quote published cases in order to supply examples of the different degrees of malignancy in this series.

The following account is taken from the *Transactions of the Pathological Society of London*, vol. x. p. 244.

(9) *Myeloid Tumour of the Fibula. Amputation; recurrence in and near stump; removal; death; metastatic deposits in lungs.*

"D. R., æt. 30, was first admitted under Mr. Cock into Guy's Hospital, in September 1854. He was a farm labourer, and had always enjoyed good health until seven months before, when he perceived a lump growing on the outside of the left knee. He had had no blow, nor could he ascribe its occurrence to any cause. It gradually increased, and during the last three weeks he had been unable to walk, from pain in the leg. On admission, he appeared to be in perfect health, but on the outer side of the left knee, and extending back into the popliteal space, was a tumour; this was punctured, but nothing but blood was evacuated. On the 7th of October, the limb was amputated above the knee, and on a section being made, the tumour was found to be a well-marked myeloid one developed in the head of the fibula. It was round, measuring four inches and a half in diameter, and consisted of a fibrous capsule continuous with the periosteum, which formed the bulk of its circumference; the cartilage completed it on the side of the knee-joint, which was quite healthy, and at the lower part the fibula ended abruptly by a jagged edge in the midst of the tumour. The interior was of a dark-red colour resembling a spleen, was composed of a fibrous matrix, which contained within its meshes the peculiar red myeloid matter, and which, under the microscope, displayed the characteristic polynucleated branching cells. The stump healed, and the man left the hospital perfectly well, to resume his agricultural employment.

"On inquiries being made from time to time, it was learned that the man's health was excellent, when, about two years afterwards, on the 20th of October 1858, he again came to the hospital with some tumours on the stump. He stated that he was in perfect health, as he appeared to be, but, about a fortnight previously, he accidentally discovered these lumps on his thigh. There was one about the size of the closed fist on the inner side, and two smaller ones on the outer side. The latter were removed by Mr. Cock, and found to resemble in every respect the original myeloid tumour, except in the fibrous matrix; the colour was red and composed wholly of myeloid matter; a part of the containing cyst was ossifying. When the wound was healed, on the 23rd of November the large one was removed, and this, like the others, consisted of a thick-walled sac, in part bony, and containing myeloid matter, in the midst of which were a few sanguineous cysts. This tumour was close to the bone, but did not actually touch it. The man died three days afterwards of acute pleurisy, when, most unexpectedly, similar myeloid tumours were found growing from the lungs. They, on section, presented the well-marked characteristic hue, and resembled the other tumours; each lung contained three or four, one being as large as the heart. Their mode of growth was peculiar in not infiltrating the texture like cancer, for they grew from the circumference

of the lung, and were pendulous, and probably would have been pedunculated, if not developed in a confined space; their shape was also peculiar in being polygonal, having flat surfaces like the lung itself, and thus indeed they looked like supernumerary lobes. The surfaces of the organs contained a few very minute deposits of the same. All the other organs were healthy, and the lymphatic glands were quite unaffected."

"As the various forms of tumours are not yet accurately defined, and opinions vary as to what constitutes a myeloid tumour, so the interest attaching to this case will vary. If the mere discovery of some myeloid cells by the microscope be not sufficient to give this distinctive name to a new growth, but a peculiar mode of formation as a gradual increase from the centre of a bone and not a mere outgrowth, and having certain naked-eye appearances which liken it to a spleen, and render it at once recognizable, then probably this is the first case recorded of a pure and simple myeloid tumour that has recurred after removal."

"Dr. Wilks, the 21st of December 1858."

(10) *Myeloid Tumour of the Humerus of five years' growth. Excision of affected part of bone; local recurrence; death from hæmorrhage; secondary deposits in the lung.*

The following is Mr. Jonathan Hutchinson's "Index to Case" in *Transactions of the Pathological Society of London*, vol. viii. p. 346:—

"Supposed fracture of the neck of the humerus in a young woman. Permanent loss of motion, and gradual enlargement above the part. Amputation at the shoulder-joint advised fourteen months after the accident, on account of a large tumour which had formed; refused by the patient. Arrest of growth in the tumour for four years. Subsequent rapid growth and enlargement of glands. Resection of the upper third of the tumour (myeloid and fibroplastic) and of the diseased glands (fibroplastic). Recovery, with a useful arm, but rapid reproduction of the disease in four different parts. Death five months after the resection from an enormous mass of sloughing and bleeding cancer. Post mortem—Cancerous growths connected with the bone, in the axilla, in the cervical glands, and in the lung."

(11) *Fibroplastic Tumour of the Humerus, containing myeloid cells. Amputation at the shoulder-joint; recurrence of the disease; death three months after the operation; secondary tumours in the lungs.*

The following account is taken from the *Transactions of the Pathological Society of London*, vol. ix. p. 367:—

"M. A. P., æt. 43, the wife of a labouring man, mother of three children, the youngest 5 years old, was admitted into the Middlesex Hospital on the 8th of September 1857. Her general health had been good, but for upwards of twenty years she had suffered from rheumatic pains in various parts of the body, which seemed latterly to have settled in the right shoulder.

"About twelve months before her admission, she began to complain of a dull, heavy pain, apparently deeply seated, in the right shoulder-joint, which at first was only felt occasionally, but was always increased by continued exertion.

After continuing for six months, the pain had assumed a lancinating character and, as she expressed it, 'frequently shot down to the tips of her fingers,' having, during the last three months, become so severe as to prevent motion of the arm.

"About two months since, she first noticed a swelling at the back part of the joint, which has gradually increased in size, and has extended all around, whilst, at the same time, the pain has become more acute than ever, so as to deprive her of rest, either by night or day.

"The treatment until of late had, apparently, been directed to 'supposed rheumatic inflammation of the joint,' but, having become an inmate of the London Hospital, she was advised to submit to amputation, which, however, she declined to do.

"When received into the Middlesex Hospital, the shoulder was so exquisitely tender as almost to prevent examination, but it was found that the circumference of the right shoulder at the highest point at which it could be measured was twelve inches, whilst the left was only nine inches; and a vertical measurement passed from the axilla and over the shoulder gave fifteen inches and three quarters on the one side, as against thirteen inches and a half on the other.

"This enlargement was not uniform, for on the outer side, in the situation of the greater tuberosity, there was a hard boss or knob which was acutely sensitive. There was no glandular affection or evidence of internal disease, but the patient's health was much deteriorated by her extreme suffering, and as the affection appeared to be limited to the humerus, amputation at the joint was proposed and readily assented to by her.

"The operation was performed on the 10th of September 1857, and presented no feature calling for observation, except that there was an unusual facility in passing the knife across the joint for the purpose of forming the inner flap, arising, as was subsequently ascertained, from the fact that the humerus had undergone spontaneous fracture just below its head, so that the knife had passed between the two surfaces of the fractured bone.

"The remaining portion of the head was readily disarticulated, when the glenoid surface of the scapula and all the surrounding parts were found—so far as examination with the finger and by the eye could determine—to be perfectly sound."

"*Examination of the Tumour removed by amputation.* — The upper extremity of the shaft of the humerus was occupied by a tumour the size of an orange, nodulated, very firm, smooth, and covered with a layer of dense areolar tissue. A perpendicular section through the tumour and humerus showed that much of the growth was composed of dense osseous tissue, and the lower part of firm, whitish, fibroid substance, which shelved off towards the top of the growth. A soft, reddish substance occupied the medullary cavity, and extended into the tumour, but the smooth margin of the proper osseous boundary of the medullary cavity of the humerus could be traced upwards into the tumour. The head of the humerus was reduced to a mere shell of bone, filled with the soft reddish substance, through which its connection with the shaft had been broken just at the anatomical neck, but the external part of the head of the humerus was perfectly smooth and sound, and covered with cartilage.

"*Microscopical Examination of ditto.*—The external portion of the tumour is composed almost entirely of fibroplastic tissue, the major portion being made up of many white fibres, interlacing in all directions as in an ordinary

fibrous tumour. Nuclei are very abundant, and are generally arranged lineally. The nuclei themselves are oat-shaped.

"A few myeloid bodies are seen in those parts of the external portion of the tumour next to the bone.

"The internal or soft portion of the tumour, situated within the head of the humerus, is highly vascular, so that under the microscope an enormous number of blood-corpuscles are seen. The tissue itself is composed almost entirely of myeloid bodies (Fig. 78, 7), some of these being small, and more or less spherical or ovoid, containing eight to ten nuclei. The majority, however, are much larger, presenting the most irregular shapes, and containing as many as twenty or thirty nuclei. A cell wall is seen to surround many, but not all, of the myeloid bodies.

"The remaining portion of the soft tissue is made up of a granular matrix, in which are embedded—first, cells similar to the nuclei of the myeloid bodies; and second, fusiform or fibroplastic cells."

"The stump healed kindly, and on the 21st of October, between five and six weeks after the operation, the patient left the hospital in tolerably good health. Even at this time, however, there was a suspicious degree of tumefaction about the shoulder. On the 16th of November, about eleven weeks subsequent to the operation, the patient returned to the hospital in a condition of great suffering, and with her health completely broken down. The soft parts of the stump had undergone great increase of size, and a portion of the cicatrix had opened, and was discharging a fœtid, watery, sanious fluid. The principal swelling was situated at the outer angle of the stump, and was covered by tense, shining skin, traversed by enlarged veins. The patient suffered from constant severe pain, of a stabbing nature, especially about the clavicle, which was uncontrollable by any means that could be devised, but she appeared to derive some comfort from the use of the extract of belladonna smeared over the origin and along the course of the brachial plexus.

"The tumour continued to grow until it assumed a globular form, and attained the dimensions of a full-sized fœtal head, the discharge became more profuse and more fœtid, and on the 16th of December the patient expired, worn out by perpetual pain."

"*Post-mortem Examination*, twenty-four hours afterwards.—The right shoulder is occupied by a tumour the size of an eight months' fœtus head, and there is a large ulcerating and sloughing surface, corresponding to the cicatrix formed after the limb was amputated at the shoulder-joint four months ago. This is formed principally of a bony mass, which is connected with the scapula; the axillary glands are involved in the mass, but they cannot be made out distinctly.

"On section, nearly three-quarters of the tumour is occupied by a loose cancellar, osseous structure, which can, however, be cut without much difficulty by an ordinary scalpel. The osseous structure is separated into nodules, each about the size of a walnut, by bands of fibrous structure, which constitute the boundaries of cyst-like cavities.

"Within the chest are considerable and extensive adhesions of both pleuræ, especially of the left, and there is some emphysema of both lungs. On making a section of these organs, a number of small, whitish nodules

presented themselves. They vary in size from a pin's head to a pea; most of them were near the surface, but were external to the pleura. Some were an inch or more deep from the surface, and they were in number not less than twenty or thirty in each lung.

"There was no other noticeable disease in any of the other internal organs, but the heart had been the subject of valvular rheumatic deposit.

"*Examination of the Secondary Growth from the Shoulder.*—The tumour, of about the size of a fœtal head, was connected with the neck of the scapula, and had grown from its outer surface. It is composed of ossifying fibrous structures, arranged in bosses, the division between them being formed by dense, fibrous septa. The major portion of the growth is surrounded by a cyst wall, composed of dense tissue; but at the internal portion, closely connected with the front of the neck of the scapula and the glenoid cavity, it is continuous with the periosteum and bone. Most of the ossified bosses have only a loose connection with the septa enclosing them, so that they separate easily, and leave corresponding cavities. In the majority of these the bone is loosely cancellous, mixed with abundant soft tissue of deep-red colour, but in some parts the bone is almost as dense as in the original tumour. When the section was first made the tumour presented the appearance of having been, in various places, the seat of hæmorrhage, for loose clots of blood lay between the ossifying bosses of the septa, which divided them from each other.

"*Microscopical Examination* of the tumour, in connection with the scapula.—On cutting a section of a moderately firm, but not ossified, portion of the tumour, it is seen to be made up of closely packed nuclei and cells, which are supported in a matrix. The matrix has a gelatinous appearance, and is finely granular, but after being kept for some little time the granularity greatly increases.

"The nuclei and cells are very various in size and form, the majority, however, are more or less oval, and about $\frac{1}{1000}$ inch in their long diameter. Some, however, are as small as one-third of this diameter, and others again are two or three times as large. The smaller nuclei are rather more spherical than the larger ones, which present great irregularities of form. The smaller bodies (the nuclei) consist of a distinct cell wall, and contain granular matter, with frequently one or two granules of large size, or perhaps a nucleolus. The larger bodies supported by the matrix are true cells, and consist of a cell wall, and are irregular and frequently angular in form; and they contain usually a single, but sometimes more than one, nucleus similar to those which are free. These nuclei sometimes contain nucleoli.

"There are also many 'fibroplastic' cells and other cells, which approach in character to the fibroplastic cell. These are extremely elongated cells, some being simply fusiform, but the extremities of others being fractured. They mostly contain a single oat-shaped nucleus.

"In addition to the above varieties of cells, the 'myeloid' bodies or cells are found in nearly all parts of the tumour. They are large masses of granular matter, in most instances surrounded by a distinct cell wall, but the envelope cannot be demonstrated in all cases. The cells are subject to great varieties in form, the smaller of them being more or less ovoid, whilst

the larger are much fractured after sending out long processes in various directions.

"In the interior of these myeloid bodies there are numerous nuclei, varying in number from three or four to thirteen or fourteen; the nuclei are rather larger than blood corpuscles, and are very granular.

"Such is the general appearance of the firmer portion of the tumour from the scapula, but, in a few places, the matrix which was first spoken of has a fibrous appearance, resembling connective tissue in the process of formation. Although the fibrous character is strongly marked in many situations, there is very little of the well-formed wavy tissue that was seen in the original tumour which was removed by operation.

"*The softer Portions of the Tumour.*—The softer portions are made up of precisely the same elements as the firmer portion, these elements, however, are arranged in somewhat different proportions. There is little, if any, of the fibrous structure, whilst the cells are in great abundance. The myeloid cells especially are numerous in the softer portions of the tumour (Fig. 78, 8).

"*Ossifying Portions.*—The portions of the tumour which are the seat of calcification exhibit some little difference of structure, which appears to depend on the amount of fibrillation which has taken place in the matrix. In the places where the fibrous structure is well marked the calcareous matter is deposited in the fibres, and the tissue has the appearance of being made up of a number of parallel cells of calcareous matter. In other places, which are chiefly composed of cells, the matrix is the seat of calcareous deposit, the cells apparently escaping from this degeneration, and remaining as spaces amid the calcareous material, standing therefore in the same relation to the osseous structure that lacunal cells do to bone. No portions, however, exhibited any appearance of canaliculi (Fig. 78, 9).

"*Tumours in the Lung.*—The tumours from the lung exhibit very little fibrous arrangement in their structure, but are chiefly made up of cells and tubes, similar to that in the shoulder. The 'myeloid' cells are not so numerous or so large as those in the larger tumour (Fig. 78, 10). The osseous portion is, moreover, similar in structure to the tumour in the shoulder.

"*Observations.*—The foregoing case is of great interest and importance from a surgical and pathological point of view, because it shows that the so-called 'myeloid tumour' may run a course which cannot be distinguished from that of the most malignant cancer. The microscopical examination of the original tumour left no doubt as to the myeloid nature of the disease, and the surgeons present at the operation of amputation at the shoulder-joint expressed a confident opinion that the whole tumour had been removed, together with the humerus to which it seemed to be exclusively confined. Notwithstanding this, in the course of eleven weeks a similar tumour grew from the scapula, and after the patient's death myeloid tumours were found in the lungs. The result of the case is disappointing to those who were inclined to accept the explanation, that those quasi-malignant tumours of the extremities, in which amputation has formed a permanent cure, have in reality been examples of innocent kind of tumour,

fittingly denominated 'myeloid.' Such tumours were first clearly described by Lebert, under the title of fibroplastic growths; and the characteristic myeloid cells were described and figured in his plates, although he does not seem to have been aware that the cells are similar in appearance to the polynucleated cells of the marrow and diplöe of bones.

"The case just related, as well as the one detailed by Mr. Hutchinson, in the last volume of the Society's *Transactions*, show that Mr. Henry Grey is in error in the conclusion to which he arrives in his paper on myeloid tumours in the *Medico-Chirurgical Transactions*, that they 'are not malignant, and when entirely removed, never return'; indeed, two of the cases narrated by Mr. Paget, in the chapter in his *Lectures on Surgical Pathology*, in which he first proposes the employment of the term 'myeloid,' would have seemed, *à priori*, to have thrown considerable doubt upon Mr. Grey's statement.

"It is remarkable, however, that these myeloid cells should have been found in so many of the cases of amputation of limbs for supposed malignant disease, in which the operation is known to have been successful; but the question now arises, whether they indicate anything more than that ossific changes are occurring in a tumour? in which case they will be found indifferently in malignant and in innocent growths. Subsequent experience may enable us to determine the exact import of myeloid cells, but at present it seems to me premature to elevate a characteristic which may, after all, only be accidental, into the test of a radical difference in the nature of a tumour. For the present I should prefer to retain the term fibroplastic as originally employed by Lebert, and to add, if the fact were so, that the fibroplastic tumour was associated with the existence of 'myeloid cells.'

"I wish to express my sincere acknowledgments to Mr. Sibley for the careful microscopical examination which he kindly made of these tumours, and to Mr. Flower for his drawings of the appearances which they presented. The testimony of two such accurate observers is all that can be required to attest the correctness of the microscopical facts related above."

"Mr. Mitchell Henry, 20th of October 1858."

(12) *Central Sarcoma of Head of Tibia, of four months' standing. Amputation; death a few months afterwards; secondary deposits in brain.*

The specimen from which the photographs (Figs. 79, 80) were taken is in the Museum of the R.C.S.Ed. (6. 442).

"Four months before admission to the Royal Infirmary, Edinburgh, the patient—a girl æt. 19—had felt a pain below the left knee. A swelling appeared, which was blistered without benefit, then poulticed and incised; but only blood escaped. The pain returned nine weeks after the opening had healed. There was by this time a distinct hard lump, which gradually enlarged. On her admission to the Infirmary, on the 10th of September, the swelling lay midway between the tibia and fibula, about one and a half inches below the level of the head of the fibula, but apparently unconnected with either bone. The swelling was blistered and then incised, but blood only escaped, and the wound thus made rapidly fungated. Amputation above the condyles was performed by Mr. Cathcart on the 19th of September 1888.

"The patient left the hospital apparently in good health and spirits. A few months afterwards, however, she became exceedingly peevish and fretful, and, after emaciating rapidly, died with symptoms of a cerebral tumour. No post-mortem examination was obtained. A secondary deposit of the tumour had probably attacked the brain."

"The section shows a soft tumour invading and replacing the cancellous tissue of the head of the tibia, and infiltrating the soft textures outside."

The microscopic character of this tumour (Fig. 79) closely resembles that of a rapidly-growing portion of some of the myeloid tumours previously illustrated; thus there are round and spindle cells, and here and there apparently abortive giant cells. These appear in two forms:

(i) Cells larger than the rest, with one or two nuclei, and

(ii) Groups of cells or nuclei, like those found in a myeloid cell, only without any protoplasm binding them together.

(These points, however, cannot be made out properly with a low power of the microscope.)

See also No. (11), Fig. 78, 8 and 10.

(13) *Central Sarcoma of Femur. Six months' growth; spontaneous fracture; amputation; death from shock.*

The specimens from which the photographs (Figs. 81, 82, 83) were taken are in the Museum of the R.C.S.Ed. (6. 445; 6. 447).

"The patient, æt. 22, a butcher, tall (six feet) and thin, and seems to have rather overgrown himself. Still, he has been always healthy enough, though rather subject to colds. His family history is good.

"In the end of February 1891 patient had 'sciatica-like' pains in the left thigh, chiefly in the knee, and occasionally running up to the thigh. He rubbed in a strong embrocation, and poulticed the painful places at times. On the 6th of July the pain became much worse, and Dr. M. was summoned. He gave him some medicine internally, and a liniment for the leg, which eased the pain during severe attacks. The pain was intermittent, worse at night, and at times very severe. It prevented him from attending to his work. On the 13th of July he had improved, and went back to work. The leg felt stiff, and he limped a little, but the pain was gone as long as the leg was kept quiet. But a slight jerk would cause intense pain, running down the front and inner side of the thigh. On the 13th and 14th of July he continued at his work, which required him to be on his feet for nearly the whole day. On the 15th he went to work, but the pain came on in the thigh so severely that he had to go home. Dr. M. ordered rest, and he has remained in bed ever since, rarely sitting up for an hour or two at a time. The pain continued severe.

"On the 16th of July a little lump appeared on the side of the thigh, about three inches below the great trochanter. This soon disappeared with rubbing. But at this time the pain was severe up and down the thigh and leg, sometimes into the foot, but always most severe at the knee.

"On the 29th of July (at 11.30 a.m.) patient was lying on his back in bed, with his left leg drawn up. He was in the act of turning on his side, when he felt the thigh give a great crack in its upper third. The pain was intense, causing him to 'roar out' at the time, and it remained severe for some time

afterwards. On the morning before the crack, the patient had noticed a slight diffuse swelling of the thigh. After the crack, the swelling quickly increased, till in three days it had reached its full size. At this time several injections of morphia were given, and the thigh was rubbed well with a liniment. The pain gradually decreased, and on the 13th of August he was free from pain, except when he gave the leg a jerk.

"On the 18th and 19th of August he had slight sciatica pains in his foot.

"On the 21st of August an exploratory incision was made, and the previous diagnosis of sarcoma of bone was confirmed.

"On the 25th of August Mr. Cathcart amputated at the hip-joint. The patient bore chloroform badly, and had to be stimulated several times with ether.

"Comparatively little blood was lost, and the patient did fairly well until 7.30 p.m., when he began to collapse, and died at 11 p.m. No post-mortem examination was obtained."

"The section (Fig. 81) shows that the tumour must have begun in the centre, just below the level of the great trochanter, where the bone is destroyed. It has extended down the medulla, and upwards into the cancellous tissue, but its chief growth has been outside the bone, entirely surrounding it, and infiltrating the adjacent muscles, although at places there is the appearance of a capsule. The upper fracture must have been the spontaneous one recorded in the history. The lower fracture was accidentally produced in preparing the specimen, but the bone was greatly weakened there by the disease. The substance of the tumour, when fresh, had a consistence and appearance like the white substance of the brain, except that at certain places it was more vascular. Microscopically, this is a large round-celled sarcoma. In many places the cells are arranged in clusters like the nuclei of giant cells, but without any binding protoplasm (Fig. 83).

"The only change produced in the bone by the growth of this tumour is absorption, both in the interior and outside. Apparently the growth was so rapid that there was no time for any reactionary development of bone from the healthy parts, while the tumour itself has not been of the bone-forming kind."

(14) *Sarcoma of Head of Tibia; three months' growth. Amputation; death a few days later; dissemination in the liver and lungs.*

The specimen from which the photographs (Figs. 84, 85, 86) were taken is in the Museum of the R.C.S.Ed. (6. 424).

The following account is taken from Sir Charles Bell's *Surgical Observations of Cases in the Middlesex Hospital, etc.*, 1816, p. 390 :—

"French Ward (Middlesex Hospital). James Lewsley, æt. 17. I observed this young man in the waiting-room as an out-patient. He said his friends alarmed him by saying that he was going to have a white swelling in his knee. I found a disease, not in his knee, but in the head of the tibia, a tumour which to the eye appeared like a swelling over the bone; but which, on examining it more particularly, was obviously attended with an enlargement of the bone. Three months before this he had experienced a slight pain on the inside of the knee and head of the tibia, and it has continued till the present.

"From the moment I saw this patient I felt anxiety for him, and pointed

out to the pupils that this was a tumour forming within the bone, and not a scrofulous enlargement; and desired that they should watch it, as in all probability it would prove another example of the fungus hæmatodes.

"For some weeks this patient was treated as for inflammation of a bone, by repeated application of leeches and blisters on alternate sides of the head of the bones; for presently it appeared that the heads of both the tibia and fibula were affected. By this means the general swelling was diminished, but on the outside, immediately below the patella, there remained a tense elastic swelling, resembling in some degree an enlarged bursa. Leeches were again applied, and an issue made by caustic. But these means, added to opiates and sudorifics, had no effect in arresting the progress of the tumour, for the swelling had assumed a form which authorized that name. The opening by the principal caustic became an ulcer; that is to say it showed a peculiar character, and began to widen. And observing that the leg had become œdematous, and that the tumour of the bones enlarged, and the ulcer had probably a connection with the disease of the bone, I took the lad into the house on the 22nd of August.

"31st. The tumour has increased in an extraordinary degree; it is larger than the first, and quite open and full-blown, like a flower (Fig. 84). In its substance it is spongy and soft, and easily broken down; in colour it is cineritious, like slough, and bloody. It bleeds on being roughly treated, but has no sensibility. The young man's health begins to break. He has been informed of the change which would take place, and now it has come he stands prepared for the worst, and has consented to lose the limb. A cold lotion has been constantly on the limb, yet the tumour has increased with remarkable rapidity; it is of the size of both fists, and embraces the heads of the tibia and fibula. The leg is œdematous and the integuments inflamed.

"The limb was amputated about the 6th of September.

"20th. He has had a restless night; his pulse is quick (100), and his tongue white; he was attacked with a rigor, which has been succeeded with heat. He is very sick, and cannot retain anything on his stomach, and his countenance is sunk.

"*Observations at Evening Lecture.*—You have seen that I examined this patient very particularly to-day, and indeed his situation is very interesting; you may have seen that the stump looks well, the ligatures long since removed, and the wound contracted. There does not seem, therefore, any source of irritation in the stump. Whence then arises his present condition? He daily wastes away, and is very thin: he has shiverings followed with flushes, his tongue is white and he is covered with perspiration, and there is a slight yellow tinge on his skin. Such an attack will sometimes precede the opening and disorder of a stump about the ninth day after the operation; or the patients in hospital will be affected by the crowded state of the house. I wish I could so consider the present attack, but I fear it is from another cause—from the irritation of internal disease.

"These symptoms increased, with the addition of pains in the right side, and heaviness in the stomach. The patient gradually sank, and died on the 24th."

"*Post mortem.*—The right side of the liver was much enlarged, and the surface was like variegated marble. There were spots of a bright yellow colour, from the size of a pin's head to that of the point of the finger. These spots were in clusters, and such parts of the liver felt soft, and around these spots there was a vascular structure, deeply stained with blood.

Similar spots of disease were seen on the lungs, and some of these were of a vascular, soft texture, having the peculiar substance of the soft cancer intervening."

There is difficulty in being sure of the exact nature of this tumour. Sir Charles Bell believed it to be central in origin, and the microscopic characters seem to confirm this view; on the other hand, there is no absorption of the cancellous tissue such as one generally sees in rapidly growing central tumours. Possibly it has begun in the cancellous tissue near the surface of the head, and having burst through the bone has then grown chiefly outwards, the growth inwards being more in the form of infiltration. It is right to observe, however, that this infiltration of the bone is more often seen in periosteal sarcomata.

The microscopical structure (Fig. 86) closely resembles that seen in some of the preceding central tumours.

Remarks on the three preceding Gradation Series of Tumours.—Every effort has been made to obtain a clinical record of the patients, both before and after operation, with only partial success. Still, there are a sufficient number of specimens to which clinical histories are attached, to make the gradation series feasible. The introduction of specimens whose clinical histories are imperfect, or absent, seems to be justified by the resemblances which these specimens bear to those which are better authenticated. In spite of imperfect records, and perhaps sometimes of an insufficient number of links in the chain, it is hoped that the following points have been brought out in the three series now detailed:—

I.—That the grades in malignancy are—

(i) Excessive local growth.—1st Series, Nos. (6), (7), (8); 2nd Series, Nos. (3), (4), (5); 3rd Series, Nos. (4), (7), (8).

(ii) Local dissemination.—1st Series, No. (9); 2nd Series, Nos. (7), (8); 3rd Series, No. (9).

(iii) Dissemination by the blood-stream.—1st Series, No. (10); 2nd Series, Nos. (11), (14); 3rd Series, Nos. (9), (10), (11); and

(iv) Local infiltration, recognizable by the naked eye.—1st Series, No. (10); 2nd Series, Nos. (15), (16); 3rd Series, Nos. (12), (13), (14).

Had epithelial tumours been included in the gradation series, corresponding differences in the mode of dissemination would have been observable.

II.—That the naked-eye and microscopic characters of the tumours which form the intermediate members of each series vary very much in different parts. This can be seen by looking over the illustrations, even although only a small portion of each tumour, as seen by the naked eye or by the microscope, has been represented.

Some parts of these tumours seem to be more, and other parts less, malignant in structure. Moreover, a gradual transition between the different parts can be traced, sometimes by the naked eye, sometimes also by the microscope. Were it not for this evidence of gradual transition, a mixture of two different kinds of tumour, distinct from one another, might be said to exist in certain individuals. Instead, however, of this being the case, a

gradual transition, like that which can be traced in a series of different specimens, can also be recognized in the structure of the individual tumours. The place of each tumour in the scale of malignancy will be determined by the clinical behaviour of its most malignant part, in spite of its having at other parts the structure, and probably the behaviour, of an innocent tumour. Consequently, the principle on which parts of the tumours have generally been selected for microscopic examination, has been to take the apparently more rapidly growing parts of a slow-growing tumour and the apparently more slow growing parts of a rapidly-growing tumour. In this way we can often trace resemblances which would not be so easily observed in parts which represent more correctly the average structure of the whole.

In order to strengthen confidence in the soundness of the three gradation series which have been illustrated, I propose next to show that the view that there is a gradation in malignancy has been held by many different pathologists, and with regard to many different kinds of tumour.

IV.—Fibrous Tumours.

Professor Virchow, in speaking of this class of tumour, said: "It is a matter of great importance to remember that the boundaries of tuberous fibroma are not clearly defined from those of other tumours, especially those of sarcoma, there being undoubtedly transition forms which existed between them" (*Krankhaften Geschwulsten*, Bd. i. p. 348).

Again, the well-known class of "recurrent fibroid" tumours affords a very good example of local dissemination. These tumours have been fully described by Sir James Paget (*Lectures on Surgical Pathology*, 3rd ed., 1870, p. 597). Examples are also given by Professor Spence (*Lectures on Surgery*, vol. i. p. 111), by Professor Chiene (*Trans. Med. Chir. Soc. Edin.*, vol. iv. p. 178), and many others.

In some of these the tumours were at first firm and fibrous in character, and became softer and more embryonic in microscopic character in subsequent recurrent tumours; in others they were soft from the first, and had the structure of spindle-celled sarcomata.

The very variety of these recurrent fibrous or fibroid tumours seems to point to their not being a special class by themselves, but only examples of different degrees of malignancy—links between the innocent fibrous tumours and the well-marked malignant sarcomata.

V.—Renal Growths.

Kelynack, in his work on *Renal Growths*, points out that "no very definite line can be drawn between the various forms of adenomatous growth. They shade off one into another. Some, especially the 'trabecular cystomata,' as they have been termed, with papillary ingrowths, are particularly prone to take on indefinite growth and to manifest malignant characters. This seems to have been recognized by several pathologists.

"Dellafield has pointed out that sometimes adenomata behave like malignant growths, especially those forms which are very vascular. As he

well says, 'The adenomata, which run a malignant course with the formation of metastatic tumours, are often called carcinomata.' Ricker has also met with a malignant form of trabecular cystoma. It is of very great practical importance to remember that, although from their microscopical characters they might be considered simple, yet frequently they prove malignant This was well illustrated in a case recently recorded by Willet."

VI.—Tumours of the Breast.

So many varieties of tumour of the breast occur, that the task of tracing the steps which lead from the innocent to the malignant forms of tumour is a very difficult one, and has not often been attempted. Three authors, however, Professor W. S. Halsted, Mr. Thorburn, and Sir James Paget, may be quoted in support of the view that tumours intermediate in character between innocent and malignant can be found among breast tumours if only they are looked for.

Professor W. S. Halsted, in the *Annals of Surgery*, vol. xxviii. p. 557, has described a series of five cases of adenocarcinoma which seem to bridge over the interval between adenoma and carcinoma in both clinical and pathological characters. These tumours he found relatively slow in growth, tending to ulcerate rather than contract; and showing themselves apt to recur locally, although with free removal they have been apparently permanently eradicated by him. They do not seem to have produced true metastasis in the glands, only endothelial hyperplasia. In summing up, Professor Halsted says: "The adenocarcinomata which I have described, resembled on section the carcinomata and not the sarcomata; a villous or papillomatous tendency was never apparent, and not even suspected from the gross appearances of the freshly cut surfaces. Fine worm-like cylinders of epithelium could be expressed from some of these tumours, but not from all. All of these new growths infiltrated the surrounding tissues just as carcinoma does. With the microscope, the power of the epithelium to make ring-like combinations, as shown in the drawings, was very conspicuous; whereas the tendency to form villous growths was not so evident."

In a short paper in the *Illustrated Medical News*, vol. iv. p. 253, Mr. W. Thorburn describes the minute anatomy of a number of cases of breast tumour, in many of which combinations of character are shown. Thus, a cystic adenofibroma, or, again, an adenosarcoma, may become in places indistinguishable from carcinoma. These tumours he would call carcinofibroma, or carcinosarcoma. He also describes and figures a tumour, which is apparently the same as that spoken of by Professor Halsted as "adenocarcinoma." Mr. Thorburn does not give any name to this tumour or assign it a place in his morphological series, but his illustrations are strikingly like those given by Professor Halsted. The following is Mr. Thorburn's verbal description of it: "The tumour consists of a well-marked fibrous stroma, containing large alveoli, each of which was filled with epithelium of a very regular type. In these alveoli were scattered numerous small spheres, apparently homogeneous or slightly granular, around which, presumably as a result of pressure, the epithelium arranged itself in

a well-marked columnar fashion. The spheres would not stain with any reagent." These spheres are not spoken of by Professor Halsted, but they are figured by him. They might be considered to be the result of abortive attempts at secretion. Thorburn states that clinically this tumour showed no tendency to be malignant. When removed, it had been growing for some two years; it was of about the size of a pigeon's egg, and there was no enlargement of the lymphatic glands of the axilla. The patient was single, and about forty-five years of age."

Besides the common acinous cancer, the rarer tubular or duct cancer is recognized as a quite distinct variety. The innocent form of this type of tumour is the "villous papilloma," also called "proliferous cyst," and Sir James Paget mentioned several instances of "recurring proliferous cysts." He made the following comment upon them: "Now if, as I believe, all these cases, and others that I have not seen, are examples of the proliferous cystic disease of the breast, they prove such an inveterate tendency to recurrence in this disease as is scarcely surpassed by any, even of the well-marked malignant tumours. Unfortunately, no examination of any of the cases was made after death; so that it is not possible to say whether the more characteristic features of malignant disease existed, such as a concurrence of similar disease in internal organs."

Remarks.—It is interesting to observe that both Sir James Paget and Professor Halsted drew attention to local recurrence as a clinical feature which enables certain breast tumours to act as links between innocent and malignant tumours.

Local recurrence showing itself in a *number of cases* seems to point to the presence of local dissemination, and this, as was pointed out in the gradation series, may be taken as a character of a milder degree of malignancy.

VII.—Cystic Tumours of the Testicle.

After careful study of a series of these tumours, Mr. F. Eve comes to the following conclusion regarding them: "There is no genetic difference between the innocent and malignant cystic tumours of the testicle; they are merely varieties of the same form of tumour" (*Trans. Path. Society*, vol. xxxviii. p. 213).

VIII.—Multilocular Cystic Epithelial Tumours of the Jaws.

In the "Erasmus Wilson Lectures" delivered at the Royal College of Surgeons of England in June 1882 (published in the *British Medical Journal* in January 1883), Mr. F. Eve gave the result of a careful study of these tumours, and made a valuable contribution to our knowledge of their true nature and varying forms. On the subject of their relative malignancy, he makes the following remarks: "The general impression formerly existing that all the multilocular cystic tumours are innocent, is entirely unfounded. Recurrence has taken place in many recorded cases after the cysts have been opened and their contents sponged or imperfectly gouged out. In a case treated in this manner by Syme, recurrence took

place twice. The more radical gouging operation recommended by Mr. Butcher is, he tells me, perfectly successful in his hands; 'the gouging,' he writes, 'must be carried out fearlessly, and far wide of the disease.'

"Recurrence sometimes takes place after the complete removal of the affected portion of the jaw. Here is a portion of a recurrent growth removed by Mr. Heath twelve years after the tumour (No. 2203) already referred to. I have also examined a growth from the upper jaw, which recurred some years after the removal of a tumour from the same situation in a child. The recurrent growth in both cases possessed the usual microscopic characters of multilocular cystic tumour.

"In completion of the evidence showing the truly malignant nature of *some* of the cystic tumours, I am able to quote the following case, for the notes of which I am much indebted to Mr. R. W. Parker, who also gave me microscopic sections of the morbid growths.

"A rapidly growing tumour of the left side of the lower jaw was removed from a woman, æt. 60, by Mr. Jonathan Hutchinson, in the London Hospital; it had been noticed only thirteen weeks. The tumour was found on section to be soft, encapsuled, and it showed points of degeneration in its centre. The patient died eight days after the operation, of bronchopneumonia. The lumbar lymphatic glands near the suprarenal capsules were infiltrated with a morbid growth, but none of the viscera were affected. In minute structure, the tumour of the jaw consisted of columns of small epithelial cells undergoing degeneration at their centres; and the secondary deposit in the lumbar glands was the exact prototype of the primary growth. Here, then, was a rapidly growing tumour of the variety under consideration, the elements of which had become disseminated throughout the system."

IX.—Chorion-epithelioma.

Dr. Teacher has made a very careful study of this form of tumour, and has published a monograph upon it. His view is that "it seems at present impossible to draw a sharp distinction between the simple moles and the malignant moles and chorion-epitheliomata, either in respect of their early clinical history or the histological appearances" (*Journal of Obstetrics and Gynæcology of the British Empire*, July 1903).

X.—Tumours of the Bladder.

In his work on the *Tumours of the Urinary Bladder*, Mr. Hurry Fenwick makes the following allusion to villous-covered malignant growths: "On examining the cystoscopy of villous-covered malignant growths, and on analysing their clinical and operative histories, we cannot avoid the inference that they form an intermediate class between benign papilloma on the one hand and malignant infiltrating growth on the other. They resemble the former in their comparative indolency and in their superficial structures when they are in their earlier stages, whilst they are akin to the latter in their basal tissues when far advanced."

XI.—Mixed Tumours of the Salivary Glands.

There is still much difference of opinion as to the exact nature of these tumours. They contain so many tissue elements that it is difficult to say which may be considered to be the chief one. But while there is uncertainty as to their pathological nomenclature, there seems to be none as to their occasional malignancy. The following extract from Dr. Carter Wood's valuable monograph, based upon the study of a series of fifty-seven of these tumours (*Annals of Surgery*, vol. xxxix. p. 205), shows that a series illustrating gradation in malignancy could be formed quite as easily of this as of any of the preceding types of tumour.

"*General Morphology.*—The mixed tumours of the salivary glands are found, as a rule, to be encapsulated, lobular growths, with harder and softer areas, the denser portions being due, as a rule, to the presence of cartilage, or firm connective tissue. They can be divided macroscopically into three great rough groups with characteristic morphology, and, to a certain extent, with a definite clinical course.

"*First.* Very fibrous tumours with very little cellular structure, and with but very little mucous degeneration and no cartilage.

"*Second.* Very hard tumours containing large masses of cartilage, and but little connective tissue or cellular parenchyma.

"*Third.* Soft, very cellular growths with transparent trabeculæ of mucous tissue surrounding areas which are opaque and yellow, which, on microscopical examination, will be found to be dense cellular areas, the colour being occasionally, though not always, due to fatty degeneration or necrosis of the cells.

"The first and second forms are likely to be benign in their clinical course, while the third form is likely to recur locally or to run an exceedingly malignant course."

. . . . . .

"*Clinical Course.*—Considering the mixed tumours from the face and neck as a group, we may say that an average of the cases in the literature shows that some 25 per cent. undergo changes which express themselves in a clinically malignant course, while about 30 per cent. recur after operative removal, though some of these recurrences may be stayed by a second or more complete removal. The records of my own series are somewhat different. Out of thirty-seven cases in which notes of the patient's condition after operation have been recorded, seventeen, or 45 per cent., recurred locally. In four of the cases, either internal metastases were soon apparent, or the local condition was so serious that the patients either died of operative shock, as in two cases, or became inoperable from the invasion of the bone and deep tissues of the neck. Of the remaining thirteen cases, one is still alive after many operations, but will probably soon succumb to the growth, which is now beyond removal. In twelve cases, then, or nearly 33 per cent., there were local recurrences which were checked by operation, so that a second removal should always be attempted if the anatomical conditions permit of a complete removal of the new growth.

"The malignancy of these growths can be judged to a certain extent

by their slowness of growth and their physical characters. The hard fibrous and cartilaginous tumours are apt to be benign, while the soft cellular types are likely to prove malignant. But frequently a tumour which has remained for a long time quiescent will begin a most rapid growth (Case 37), and in a few months increase in size more than during its entire previous existence. This sudden and rapid growth is accompanied by the clinical and microscopical evidences of malignancy, and the tumour spreads through the surrounding tissues, involves the skin and the salivary glands, and may form metastases, changes which are illustrated by Cases 25, 28, and 36. Twenty cases out of thirty-seven, or 55 per cent., were permanently cured by operation."

It does not seem necessary to extend this list further, although there would be no difficulty in doing so.

CHAPTER III

TRANSFORMATION OF INNOCENT INTO MALIGNANT TUMOURS

THERE are two phenomena of tumour growth closely allied to one another, which may be included under the heading of "Transformation of Innocent into Malignant Tumours."

I.—Instances where a tumour, after retaining for many years the characters of an innocent growth, has changed its character and become malignant.

II.—Instances where a number of tumours of the same type of structure are present in a patient, some being innocent, and one or more malignant, in character. Those which are malignant may have been originally innocent or they may have been malignant from the first; but the history is often wanting which would enable us to judge between these two possibilities.

I.—INSTANCES OF THE TRANSFORMATION OF AN INNOCENT INTO A MALIGNANT TUMOUR.

1. *Fibroma of Scalp becoming malignant.* Museum of the R.C.S.Ed. (12. 104).

"This was one of many soft fibrous tumours which had been present from infancy in this patient. It had only begun to increase when the patient was aged 47, but it had then grown rapidly, and had broken down and ulcerated; it had been removed, and showed fibrous tissue well developed in some places, but in an early stage of development in others."

2. *Cast of a Sebaceous Cyst which became malignant.* Museum of the R.C.S.Ed. (12. 71).

"This was one of many wens which had been present on the scalp of a woman, æt. 60, for about thirty years. One of these had begun to enlarge about three months before the patient sought advice, and had rapidly involved the surrounding tissues, and caused enlargement in the glands. The case was inoperable, and the patient died in a lunatic asylum, not long after having been discharged from the Infirmary."

3. *Wart becoming cancerous.* Oliver Pemberton on *Surgical Cancer* (p. 118).

"E. M., æt. 48, single, a laundress, of dark complexion and spare habit, was admitted into the hospital in March 1861, under the care of Mr. Bolton.

"*History.*—Sixteen years ago she noticed a small wart-like growth, about the size of a pin's head, in the cleft between the second and ring fingers of the left hand. It remained the same size for five years, occasionally giving her shooting pain, more especially after being used freely in her occupation. After this it began to grow and continued to increase slowly up to Christmas last, when it had attained the size of a horse bean, and had crept round so as to be situated on the palmar surface of the cleft. During the last ten years the pain in it has been very constant, and of a sharp, shooting character. The investing skin remained quite sound until about a month before coming to the hospital, when she ran a hook in it, and the sore produced by this accident did not heal. No history of cancer in her family.

"In the month of February she came first as an out-patient. In the situation already described, and appearing to be intimately attached to the skin, was a hard immovable swelling of the size of a hazel-nut, with a small ulcerated point in its centre. An incision was made into this, but only blood escaped. The incision thus made did not heal, but gradually formed a sore, which spread rapidly, the edges becoming everted and hard, the centre excavated, the discharge thin, and the granulations small and compact.

"April 3rd.—Having become an in-patient, the second finger was amputated at the metacarpal joint, the head and part of shaft of the metacarpal bone being also removed. The wound healed for the most part rapidly, but was not quite sound when she became an out-patient—April 20th. A week or two afterwards the edges of the wound became thickened and everted, assuming the character of the sore for which the finger has been removed.

"October 17th.—Was readmitted; the ulceration having been enlarging up to the present time.

"There is now an indolent granulating wound, raised about one-third of an inch from the surrounding skin, an inch and a half broad, extending from the cleft between the index and ring fingers to within an inch of the carpal end of the metacarpal bone on the dorsum of the hand. The ulceration passes forwards to the palm of the hand, extending for a distance of nearly an inch beyond the cleft; and, indeed, occupies the exact situation of the cicatrix marking the removal of the finger. The skin around is puckered in places, and towards the edge of the sore it is of a bluish tint. She has continued stinging pain in the sore; none in the forearm or axilla. There are no enlarged glands. Has lost flesh since the pain has been so severe. Menstruation has ceased within the last six months.

"October 27th.—The forearm was amputated, and the patient was discharged, with the stump healed, November 15th.

"I lost sight of this patient for some time afterwards, and did not see her again until July 1863, when she happened to come to the hospital as an out-patient on my day of attendance. She looked ill and wasted. Two months after the amputation she found the glands at the inner side of the elbow becoming enlarged. In some few months the skin covering these gave way, and at this present time there is a vast ulcerated surface stretching half-way up the arm on the inner side, having all the appearances previously described as belonging to the earlier disease. Shortly after the enlargement and giving way

of these glands a solitary tumour—soft, round, and elastic—formed in the cellular membrane beneath the anterior fold of the axilla of the same side. This is now as large as an orange.

"E. M. died January 8th, 1864.—At this date the ulceration extended over the neck, back, and breast. The tumour, after reaching a large size, burst through the skin, and sloughed and bled freely."

4. *Mole becoming cancerous.* Oliver Pemberton on *Surgical Cancer* (p. 120).

"In June 1863, I was requested by Mr. Thomason, of Whitehall Street, in this town, to visit J. M., æt. 67, a tall, thin, pale old man, whose occupation had formerly been that of a maltster.

"From his birth there had been a small mole on the skin between the scapulæ, and from this, in the course of time, a warty substance grew, which seven years since commenced to discharge. When Mr. Thomason first saw him, in the April previously, the warty character of the growth to a certain extent remained, but there was superadded a fungous character, which produced a spongy, ragged surface, bleeding at times and discharging freely. It was as large as a hen's egg, of dark livid colour, especially around its base, which was intimately attached to the skin. In the left axilla were two glands as large as pigeons' eggs, which had formed three years back. Finding the bleeding becoming a serious loss to the patient's strength, Mr. Thomason excised the growth as well as the darkened base. The wound healed in six weeks.

"Until the end of May he seemed to improve, then a change took place; and when I saw him he was complaining of pain in the epigastrium, and was losing flesh rapidly. The liver was hard, and prominent in places, and the right leg œdematous. He sank and died on the 21st of July.

"The body was examined two days after death.

"*Thorax.*—Contents natural.

"*Abdomen.*—The liver was studded throughout with tubera of encephaloid cancer. The lumbar glands were affected by deposits of a similar character. There were no other organs involved.

"The axillary glands presented, on section, a similar appearance to the deposits found in the liver.

"The family history of this patient afforded the fact that an uncle had died of cancer of the mouth; beyond this, his predecessors had been healthy. J. M. himself had four daughters. Of these, one, æt. 43, is at present the subject of scirrhous cancer of both mammæ. A second, æt. 37, has numerous moles about the body, but is healthy, as well as her two remaining sisters."

5. *Mole becoming melanotic Cancer.*

This phenomenon has been observed by many writers. Thus, the late Mr. Oliver Pemberton in his Monograph on *Surgical Cancer* deals with "Melanotic Cancer" in one of the chapters. Speaking of the appearances which it presents in various parts of the body, he says:

"*In the Skin.*—The production of a small solitary, deep brown, black, or blackish spot, situated on some part of the skin. Very frequently this spot is located near to a congenital mole or wart, or the congenital marks themselves undergo melanotic degeneration. Thus, in thirty-four cases in which the disease appeared in the skin or subcutaneous tissue,

I ascertained that fifteen had developed in or near a congenital mole, wart, or mark." Among other examples, the following striking case is given:—

"P. C., æt. 53, a collier, married—a worn, pale-complexioned man—was admitted under my care, to the hospital, on the 24th of March 1855, having a black patch of diseased structure on the right cheek.

"*History.*—He had always, within his recollection, a mole in this situation.

"It had never occasioned him pain or annoyance until within three months of his admission. The first occasion of its doing so was after it had been accidentally wounded by a barber in shaving. After this it began to prick and shoot, and to increase slowly in dimensions. In earlier life he had been the subject of epileptic fits, but not for seventeen years had he suffered an attack. Though of delicate constitution, he had followed a laborious employment in the pits, and had encountered the hardships and accidents incidental to his occupation. He had always been temperate. His family are healthy, and there is no tendency to disease known amongst them. His wife informed me that for some months past he had been losing flesh, and had been the subject of cough and feeble digestion.

"Upon examination, the growth presented an irregular, black tuberculated patch of warty structure, situated immediately over the right malar bone. It was about as large as a florin piece, movable with the integument, with its limits accurately defined. Its surface was not ulcerated, nor was the neighbouring integument affected. Closely adjacent to its outer margin, and connected by a small intermediate portion, were two tubercles of the size of peas, which partook of the character of the larger one. The colour of these formations was coal-black, the only exception to this being a slight variation in intensity in different parts.

"The submaxillary glands of the same side were enlarged and hardened. There were no other tubercles or discolorations to be seen on his body.

"In consultation with my colleagues, we determined that no operation was advisable.

"On the 10th of April, sixteen days after admission, he died suddenly, almost without warning, and without any illness, save an increasing feebleness and some vomiting.

"The body was examined twenty-four hours after death.

"*Head.*—On examining the skull-cap, its internal surface was found to be irregularly marked by melanotic deposit; the same condition was present in the floor of the cranium. The colour of this deposit was deep black, it was scarcely raised from the surface of the bone, and whilst, in some instances, it penetrated inwards, so as to stretch across the diplöe to the external table, in others it was readily removed by scraping, leaving the bone of its natural colour beneath. Thus it diffused itself in patches of irregular shapes and dimensions in all directions. It was altogether situated beneath the pericranium. This membrane was stained by contact in some few places on its external aspect, but there was no thickening or other change apparent in its structure. The brain was natural.

"*Thorax.*—The lungs contained many nodules of melanosis. These were chiefly noticeable upon their posterior parts, and varied in size from a small pea to a cherry. They were circular in figure, intensely black in colour, and were situated mostly beneath the pleura, but were in the parenchyma of the organs as well. The lung structure around the deposits was perfectly natural, and was in immediate contact with them. The heart on its posterior as pec

was sprinkled by jet-black spots. The melanotic matter constituting them was placed beneath the visceral pericardium. It showed itself towards the right of the septum ventriculorum, being scattered mainly over the surface of the left ventricle just below the auriculoventricular furrow. It stretched over the space of an inch in length, and was at first separated into many small diffused points, of a greyish tint, and was finally gathered up into a large patch of a deep black colour. The cavities and the remaining parts of the viscus were natural.

"*Abdomen.*—The liver was a mass of melanotic deposit, three times its natural size: it extended itself downwards, and to the left side, encroaching on the neighbouring regions. The melanotic tubera were of all sizes, from the minutest speck or grain, to others as large as a pigeon's egg. They filled the organs in all directions, appearing to be inserted in the midst of the hepatic structure, which was more tawny in colour, and more friable than natural. They did not appear to coalesce with one another, but were isolated by intervening liver tissue, which was in immediate contact with their external surfaces without the intervention of a cyst. On the anterior surface, the peritoneal covering was elevated into a series of undulations, caused by the upheaving nodules beneath. Beyond being thus raised, the membrane presented no appearance of thinning. On section, the tubera had a homogeneous aspect. Their consistence varied, and was generally somewhat firmer than tallow, and they had nowhere undergone any softening. Their colour was deep black or brown, and of every shade between these two. The spleen contained similar deposits, three or four in number, of the size of swan shot. The kidneys were similarly affected. The small intestines were sprinkled in a few places. The mesenteric glands were dark-coloured and slightly enlarged.

6. *Mixed Tumour of the Parotid becoming malignant.*

The following good example is published by Dr. Carter Wood in the article already referred to (*Annals of Surgery*, 1904, p. 68):—

"Case 4.—St. Luke's, No. 1745. The tumour was removed from the left parotid region of a man, æt. 59, who first noticed the tumour fifty-three years ago. It was then the size of a small nut, and freely movable. For many years the growth was exceedingly slow, but in the last few months it has been very rapid. The ear is pushed back by the growth. The tumour is very hard and adherent both to the skin and the deeper tissues. It cannot be moved in any direction. Its surface is smooth. In the neck are a few large, hard nodes which have appeared recently. The patient's general condition is good.

"The tumour was removed with some difficulty, as it was adherent to the deeper tissues, and a large number of the cervical lymph nodes had to be removed. When hardened, the mass measured six by seven by twelve centimetres. It is pear-shaped, with the larger portion above over the parotid. The cervical fat is filled with hard, enlarged lymph nodes. The internal surface, directed towards the parotid, is rough from separation of the tumour from the underlying tissues. The outer portion directed towards the surface is smoothly encapsulated, and there is a thin capsule between the tumour and the remnants of parotid tissue. The cut section shows two different appearances. The superficial portions are transparent, with faint yellow strands running through them; the deeper are opaque and white. The nodes are also opaque and white.

"Microscopical examination of the growth shows a similar variability in the tumour. The peripheral portions possess the morphology designated as

endothelial, with a soft, fibrous stroma and long branching strands and alveoli, some of the latter filled with hyaline material. The deeper portions are composed of the same endothelial structures infiltrated with carcinoma. The carcinomatous growth resembles that of an infiltrating epithelioma rather than that of a glandular carcinoma, such as one would expect in a carcinoma of the parotid. The cells are large and flat, staining deeply with eosin. In some areas intercellular spines can be seen. Mitotic figures are fairly abundant. The parotid, which is separated from the growth by a fibrous capsule, is normal in appearance, and contains but little carcinomatous infiltration. The nodes are filled with the carcinomatous new growth, and very little lymphoid tissue remains.

"In the opinion of the writer, the best explanation of the condition is that the patient had, since childhood, a tumour of the endothelial morphology, and that the recent rapid growth is the result of the carcinomatous change which has taken place in the epithelial cells of the so-called endothelial new growth. That the carcinoma is not derived from the parotid seems probable, for the gland is not extensively invaded, as it would be if the carcinoma were primary. Landsteiner describes a similar case in which malignant changes had taken place in a chondromatous tumour of the submaxillary gland, with the formation of growths of an epitheliomatous character which had broken through the tumour capsule and infiltrated the surrounding tissues. The regional lymph nodes were not invaded, in which point the case differs from the above."

7. *Tubular Cancer of the Mamma, developing from cystic villous papilloma of long standing.*

Mr. Roger Williams (*Diseases of the Breast*, 1894), in discussing "The Question of the Origin of Malignant from Non-Malignant Neoplasms," is of opinion "that the possibility of benign neoplasms taking on malignant characters later in life, must be admitted; but this is a very different thing from admitting that such neoplasms are specially prone to develop malignant disease. This is disproved by the extreme rarity of the coincidence" (p. 317).

The following is one of two cases which Mr. Roger Williams has personally observed (p. 313):—

"A large, obese, sterile, married woman, æt. 54, thirty-four years ago noticed a tumour in the upper part of her right breast, which slowly increased to the size of a hen's egg, and then became stationary. So it remained until three months before I first saw her, when, without injury or other known cause, the tumour began to increase. In this short time it attained the size of the fœtal head at birth. On examination I found a circumscribed, bossy tumour, adherent to the overlying skin, which was reddened in places, but movable over the subjacent structures. Some of the bosses were soft and fluctuating, while others were hard. The nipple was retracted. The axillary glands were slightly enlarged, as well as those below the clavicle. There was no history of cancer in the family. The breast was amputated, and the axillary glands removed. On examination of the tumour after removal, the whole of it was distinctly encapsuled. In many parts of the capsule there were extensive calcareous deposits. On section, the bulk of it was seen to consist of large cysts, containing brown serous fluid, and there were also numerous small cysts in the adjacent parts; in addition to the fluid, many of the cysts contained villous papillary growths. At the sternal side of the main tumour was a solid, yellowish, encapsuled mass, the size of a Tangerine orange, which appeared

to be of more recent formation than the rest. Microscopical examination of a portion of this revealed duct-like structures, which often contained papillary ingrowths. Examination of the excised axillary glands revealed only inflammatory changes. It was evidently a case of tubular cancer that had developed in connection with cystic villous papilloma of old standing. Two and a half months later, recurrence was noticed in the mammary region. Seven months later the skin over the whole of the front of the thorax and upper part of the abdomen contained numerous small, hard, cancerous nodules. In the right mammary region these were confluent and ulcerated. The right axilla was infiltrated, and the upper limb œdematous. She died of right hydrothorax, with collapse of the lung, nearly seventeen months after the operation. At the necropsy, the local disease was found to have spread by direct extension through the thoracic wall to the right pleura and lung, both of which contained numerous cancerous nodules. The pleural sac contained 70 ozs. of fluid, and the lung was collapsed. There were two caseating tubercular deposits in the upper lobe of the left lung. The heart was small and fatty. The peritoneum was thickly studded with cancerous nodules. The liver was large and fatty, and the gall-bladder contained three facetted calculi. The spleen and both kidneys were congested. The uterus was small, and presented several pedunculated fibroids at its fundus."

8. *Uterine Fibroids becoming malignant.*

Mr. Bland Sutton (on *Tumours*, p. 184) narrates a well-marked case of this change as follows:—

"The most typical example of malignant fibroid which came under my notice occurred in a woman, æt. 59; she had had a fibroid in the uterus fifteen years. It had not caused her inconvenience until shortly before she came under Dr. Finlay's observation (*Trans. Path. Soc.*, vol. xxxiv. p. 177). When she died, I made the post-mortem examination, and found a pedunculated fibroid, as big as a child's head, attached to the fundus of the uterus; it was adherent to, and had penetrated, the bladder and the intestine. Secondary nodules were found at the base of the right lung and the wall of the left ventricle of the heart and in the left kidney. The microscopic characters of the tumour were characteristic of a myoma and a spindle-celled sarcoma. The secondary nodules were identical in structure with the large tumour."

Professor Senn (on *Tumours*, p. 80), under the heading of "Transformation of Benign Tumours and Post-Natal Embryonic Tissue into Malignant Tumours," says that, "as the result of some observations, the writer is convinced not only that such transformation is possible, but also that it takes place much more frequently than has heretofore been supposed." As an illustration of a benign being transformed into a malignant tumour, he relates the following:—

"The patient was a married woman, æt. 52, the mother of several children. For at least ten years she suffered from a pelvic difficulty which, six years ago, was diagnosed as a myofibroma of the uterus. Since that time she has suffered from profuse menstruation. Examination disclosed a smooth tumour occupying the middle of the lower part of the abdominal cavity and reaching as far as the umbilicus. On vaginal examination, the lower segment of the uterus was found high up and was affected by the movement of the tumour. The absence of

metrorrhagia and the clinical history spoke in favour of the diagnosis previously made. On opening the abdomen, there was found what appeared to be a large myofibroma of the uterus springing from the fundus between the cornua. The immobility of the pelvic part of the tumour induced the writer to make a more thorough examination, which revealed extension of the tumour mass from the uterus to the broad ligament on the right side. The operation proved to be a very difficult one. The entire uterus with the pelvic mass on the right side was removed. The examination of the specimen showed an interstitial myofibroma, the lower segment soft, and continuous with the extra-uterine part of the tumour. Microscopic examination of the upper dense part of the tumour showed the characteristic structure of a myofibroma, while sections from the lower part of the tumour, the infiltrated uterine wall, and the extra-uterine part of the tumour, presented the typical picture of round-celled and spindle-celled sarcoma. There could be no doubt in this case that the myofibroma had existed for at least ten years, and as the sarcoma constituted a part of the tumour, it was evident that it occupied that part of the tumour which had undergone transformation from a benign into a malignant tumour."

9. *Innocent Thyroid Tumour becoming malignant.*

The following is a quotation from Mr. Jonathan Hutchinson's *Archives of Surgery*, vol. iv. p. 65:—

"The transition from non-malignant growth, or even from hypertrophy, is, I believe, not unfrequently witnessed in the case of the thyroid gland. An instance of this I find recorded by the late Dr. Dutton of Birmingham (*Birmingham Path. Soc.*, October 5, 1844).

"A woman of 60 had been the subject of quiet bronchocele from girlhood. It had caused her no inconvenience until three months before she came under Dr. Dutton's notice. It then became very hard, and increased rapidly in size. The increase was chiefly on the left side. Both trachea and œsophagus became compressed, and she was unable either to swallow or lie down. Death from asphyxia followed in about five months from the beginning of the enlargement. The tumour on examination presented 'a soft pulpy mass of a medullary character throughout.' The late Mr. Hodgson, who spoke in the discussion, said that he had seen an exactly similar case in a man."

Mr. James Berry, in *Diseases of the Thyroid Gland*, expresses a similar view:

"Malignant disease of the thyroid gland . . . may occur in a gland that has previously been normal, but it is much more prone to affect one that has already been the seat of innocent goitre" (p. 197). He narrates the history of a case of the sort (p. 205).

10. *Innocent Adenoma of the Rectum becoming Carcinoma.*

Sir Charles Ball (*Brit. Med. Journ.*, 1903, p. 413) makes the following remarks which bear upon this subject:—

". . . and as the cutaneous wart, after existing for many years without apparent change, may spread into the deeper tissues and become a malignant epithelioma, so we find that cancer of the rectum may have been preceded for a long time by a purely benign adenomatous growth, particularly if the tumour is one of the sessile and not pedunculated varieties of simple adenoma."

11. *Innocent Bladder Tumour becoming malignant.*

Mr. Hurry Fenwick (on *Tumours of the Bladder*, p. 40) makes the following remarks under the heading of "The Gradual Transformation of a Benign Papilloma into a Malignant Papilloma":—

"I cannot say that this will be frequently encountered. Our present knowledge of these growths is as yet too immature, and the chances of error are too great to permit of any dogmatic statement as to the probability of such a change taking place in any given case; still less of the frequency with which such a change may be expected. Cases, however, occur which point to such a transformation, and we have the well-known clinical analogy of papillomata of the skin taking on malignant action.

"Although villus-covered malignant papillomata are usually more indolent in their growth than other forms of malignant disease of the bladder, yet I have met with cases eventually proving to be the former disease which have been marked by symptoms extending over twenty years. This prolonged life forces me to suspect that the papillomata were at first benign, but that bladder-fret, combined with a marked carcinomatous predisposition, gradually transformed them into malignant growths. Thus:

> "Dr. Mooney brought me a gentleman, æt. 44, who had suffered from symptomless hæmaturia for twenty-two years before coming under my observation. He had had intermissions, being in perfect urinary health for so long a period as ten years in one interval, and four years in another.
>
> "Four years prior to his cystoscopy his stream became blocked, obviously by growth occluding the vesical orifice, and the difficulty in urination culminated in retention, for which the catheter was used. Cystitis ensued, but partially subsided; it recurred, and at the fourth attack, pain in the left kidney supervened. I removed, suprapubically, a large, walnut-sized, broad-pedicled, villous papilloma from the left ureteric area, and another and smaller from the right ureteric area. The bases were succulent, and Mr. Targett reported they showed malignant characters. He recovered; but the growth returned, and he eventually died uræmic."

"A few other cases incline me to believe that the stalks or bases of those which seem to take on malignant action thicken and shorten, until the entire growth becomes subsessile or absolutely sessile."

12. *Innocent Tumours of Larnyx becoming malignant.*

In 1889 Sir Felix Semon published a monograph on *The Question of the Transformation of Innocent into Malignant Tumours of the Larynx, especially after Intralaryngeal Operations* (*Die Frage des Ueberganges Gutartiger Kehlkopfgeschwulste in bösartige*, Berlin, 1889, August Hirschwald). This was founded upon a collective investigation among laryngologists all over the world. As the title indicates, the relation of intralaryngeal operations to the possible transformation of the character of laryngeal tumours was considered of especial importance. Still, as the possibility of the transformation taking place without operation has an important bearing on the main question, this possibility was also carefully investigated. Twelve "probable cases of spontaneous transformation" are narrated and discussed in Section 9. In reviewing these, the author says (p. 107) that, "as the result of the

most impartial critical sifting of the twelve reported cases, there is only one (that of Newman's, No. 7) which is quite free from objections; two are classed as slightly probable; three as very possibly of this nature; while the remainder seem to be doubtful." He then proceeds: "But even this result is sufficient to establish almost without a doubt that in the larynx, as in other parts of the body, a transformation of innocent into malignant tumours sometimes takes place under the influence of conditions which are not yet understood, but which are at least independent of intralaryngeal operations." Dr. Newman's case was published in the *Glasgow Medical Journal*, February 1888, as follows:—

> "The other case I showed as an example of 'large adenoma occupying the upper part of the cavity of the larynx.' Subsequently I removed more than half of it by means of forceps, and as I did so I submitted piece by piece to microscopic examination. The first portions of the growth presented the characteristics of a simple adenoma, whereas the deeper portions, those which were removed last, showed the structure of an adenoid carcinoma, with unusually abundant stroma. Tracheotomy was performed in October 1885, previous to the endolaryngeal operations. Shortly after I discovered the nature of the deeper portions of the tumour, I detected an enlarged gland over the left side of the thyroid cartilage. I then discontinued the use of the forceps. The increase in the bulk of the glands was very slow, and the patient enjoyed comparatively good health till July 1886. At that time there was very little interference with respiration, but the patient experienced great difficulty in swallowing even fluid food. This difficulty speedily increased, and appeared to be due more to the enlargement of the cervical glands than to the extension of the primary growth. The tumour in the larynx underwent very little change between the beginning of 1886 and the time of his death in September of that year."
>
> Sir F. Semon wrote to ascertain definitely whether this might be considered a case—(*a*) of spontaneous transformation; (*b*) of transformation attributable to operation; or (*c*) a mixed tumour from the first.
>
> Dr. Newman answered on the 26th of April 1888: "With reference to the case of adenoma which became an adenocarcinoma, I consider it an example of transformation quite independent of operative procedure. It was ascertained that the tumour had been present in the larynx—without noteworthy enlargement—for four years before August 1885. In that month the tumour enlarged suddenly while the case was under observation, and the increase was so rapid that while it was of the size of a pea in July, by October of the same year it had grown so large as to obstruct respiration and render tracheotomy necessary. Intralaryngeal operation was only begun after that. Previously the patient had objected to every form of laryngeal instrumentation, and only yielded when respiratory difficulty compelled him. The case must therefore be considered as one of spontaneous transformation."

To this Sir F. Semon adds the following note (*loc. cit.*, p. 101):—

> "This case seems to be certainly free from objection. The fact that the tumour had been ascertained by the laryngoscope to have been present for four years, without noteworthy change, the sudden increase within a few months (which reminds one of the sudden increase of size—corresponding to the onset of malignant degeneration—in a goitre which has remained for years unchanged),

without any previous intralaryngeal instrumentation, the careful and repeated microscopic examination of every piece removed, its relative position being noted, the character of gland cancer being only recognized in the deeper parts; together with Dr. Newman's recognized competence as a pathologist; all these combine to make it evident that this must be considered a case of spontaneous transformation of an innocent into a malignant tumour of the larynx, not one which has been a mixed tumour from the beginning."

13. *Transformation of an Innocent into a Malignant Neurofibroma.*

The following extract, taken from Mr. Alexis Thomson's monograph upon *Neuroma and Neurofibromatosis* (p. 85), furnishes an interesting example of malignant transformation in another kind of tumour:—

"The frequency with which the development of sarcoma has been observed in the subjects of multiple neurofibromata indicates that the association is more than a coincidence, and has led to the conclusion that the subjects of multiple tumours of the nerves are more liable to malignant disease than other people. Garré has the credit of demonstrating that the sarcoma which develops under these conditions, and to which he gave the name 'secondary malignant neuroma,' differs in several important particulars from that which develops in nerve trunks assumed to be normal, and which has already been described with the circumscribed and solitary tumours in Chapter III. It may be repeated in this place that the primary sarcoma of nerve trunks does not materially differ from sarcomata originating in other tissues; it exhibits the same rapid growth, the same tendency to infiltrate, and the same tendency to give rise to secondary growths in the internal organs. The 'secondary malignant neuroma,' on the other hand, is characterized by the rapid increase in size of a tumour which may have been in existence for years, and it may be from infancy, by the fact that it only infiltrates the surrounding tissues when it has recurred after removal, and that the recurrence is nearly always confined in the first instance to the nerve originally involved, or to other nerve trunks, and that it either does not give rise to metastases in the internal organs at all, or only at a very late stage in the progress of the disease. These views, promoted by Garré, have been corroborated by Scheven and others. The following case, observed by the author, is absolutely typical:—

"A man, æt. 28, had suffered from multiple tumours of the peripheral nerves since the age of 13; one of them, on the right median nerve at the elbow, had increased in size and become intensely painful during the twelve months before he applied for treatment. I removed this tumour, and found it to be composed of the usual overgrowth of endoneurium, but at one point of the sections there was a decided transition to a more cellular type of tissue suggesting a spindle-celled sarcoma; the transition could be traced step by step from the branching cells of the endoneurial connective tissue. It recurred within four months, and again involved the median nerve; it was also adherent to the surrounding tissues, and had fungated through the skin; there were now evidences of paralysis in the distribution of the median nerve. The limb was amputated. The tumour was found to be an ordinary spindle-celled sarcoma. Ten months later, recurrence took place in the stump, and the limb was amputated at the shoulder-joint. The growth was again a perfect type of spindle-

celled sarcoma. Recurrence again took place in the vicinity of the scar. He lost flesh rapidly, and developed symptoms of a rapidly growing tumour in the left lumbar plexus (painful contracture of the left lower extremity, pressure on the ureter, etc.), and died a little more than two years after the first operation. On post-mortem examination, the viscera were found to be free from metastases. There was a spindle-celled sarcoma as big as a child's head involving the left lumbar plexus, the left psoas muscle, and the adjacent bodies of the lumbar vertebræ."

"This case brings out very well the salient features of the 'secondary malignant neuroma,' and illustrates in a remarkable way that the sarcoma, grafted on the fibromatosis of a nerve trunk, while identical in structure with sarcomata of other origin, and while presenting all the features of local malignancy, instead of giving rise to metastases, is followed by the transformation into sarcoma of neurofibromatous tumours in other parts of the body. There are exceptional cases recorded, however, in which there were visceral metastases in 'secondary malignant neuroma.' Hume, of Newcastle, observed one in which, after removal of a sarcoma involving the sciatic nerve from a patient, the subject of neurofibromatosis, death took place from metastases in the lung, pleura, liver, and humerus. Westphalen records another case of generalized neurofibromatosis, in which a sarcoma developed in the popliteal space; the limb was amputated at the hip-joint; metastases were found after death in the pleura and lung. A similar case is recorded by von Winiwarter.

"As regards the relative malignancy of the primary sarcoma of nerve trunks, and the 'secondary malignant neuroma,' Garré's original view was that the latter was the less malignant of the two. While this may be true as regards its capacity for giving rise to secondary growths in the viscera, it does not hold so far as the danger to life is concerned. The list of cases of neurofibromatosis in which sarcoma has supervened is one continuous record of deaths."

It does not seem to be necessary to give any more examples of the transformation of innocent into malignant tumours. Malignant growths may indeed begin as such more frequently than they begin as innocent tumours, but that does not concern the present argument. All that is here important is that the transformation does take place, and this, in the light of the evidence brought forward, does not seem to admit of any reasonable doubt.

II.—Instances where Tumours of a similar Type of Structure, but some Innocent and others Malignant in Character, have been simultaneously present in the same Patient.

In parts of the body not within sight or accessible to touch, the progress of new growths cannot be watched, and a transference from an innocent to malignant character cannot be ascertained as it can be when the tumours are in accessible parts of the body. For this reason, and also because an exact history is not always available even where multiple tumours are in accessible parts of the body, it seems advisable to form a group of cases in

which innocent and malignant tumours of a similar kind are simultaneously present. In most cases the malignant individuals in each group will probably have been originally innocent, but there seems nothing to prevent a malignant tumour beginning as such side by side with an innocent tumour of a similar kind.

Among the cases of malignant transformation already quoted, there were instances of the simultaneous presence of innocent and malignant tumours of a similar kind—as where one out of many soft fibromata (No. 1), and one of many sebaceous cysts (No. 2), became malignant.

Other examples may be found among the cases of multiple adenoid tumours of the colon and rectum. In a long paper upon this subject (*Beiträge zur klinische Chir.*, Bd. xviii. p. 356) Dr. J. Schwab makes the following remarks: "In most cases the affection extends over a very long time. The changes in the intestine take on a chronic form. Frequent improvements are often seen, so that the condition may resemble chronic catarrh of the intestine with repeated exacerbations, and this may continue for years without endangering the patient's life. Very often indeed the affection of the colon is scarcely appreciable. When the rectum is also involved, the polypi often show a tendency to undergo carcinomatous degeneration, and the patients die with the symptoms of rectal carcinoma. At the post-mortem examination colitis polyposa is discovered in addition to the rectal cancer. Schwab quotes several cases to illustrate the association of innocent and malignant new growths in the lower bowel, and of these one of the most instructive is the following. It was published by Dr. H. Handford in the *Pathological Society's Transactions*, vol. xli. p. 133:—

"*Disseminated Polypi of the large Intestine becoming malignant; strictures (malignant adenoma) of the rectum and of the splenic flexure of the colon; secondary growths in the liver.*"

"E. F., a cachectic-looking woman, æt. 34, was transferred from the surgical side of the general hospital, Nottingham, to my care in September 1889, on account of some lung affection which was diagnosed during life, and proved post mortem to be bronchiectasis of the left lung. A week previously my surgical colleague, Mr. A. R. Anderson, had removed the accompanying polypus (measuring in the spirit preparation 3·75 cms. by 3 cms., rounded in shape, and weighing 180 grs.), which was attached by a long narrow pedicle, just above a stricture of the rectum, extending from about two inches above the sphincter upwards for about two inches. The stricture would admit the index finger readily, but it was only by a great effort that the finger could be passed beyond it.

"The cough, purulent sputum, and therefore probably the bronchiectasis, had been in existence for ten years. The duration of intestinal symptoms is unrecorded.

"There was no family history of malignant disease or of intestinal polypi. She was married, had had four children, all of whom died young; no miscarriages, and no history of syphilis.

"At this time the liver could not be felt to be enlarged, the liver dullness was not increased, and no lumps could be felt, but she occasionally had pain in that region.

"On surgical grounds it had been decided that the case was not suitable for excision of the rectum, and the passage of fæces was so free that colotomy was not at that time necessary. She went home, and was readmitted in February 1890, five months later, with the stricture very tight, great abdominal distension, especially of the cæcum and ascending colon, and a greatly enlarged nodular liver, reaching from the fourth space in the nipple line to the level of the umbilicus. She died ten days after readmission.

"At the inspection, fourteen hours post mortem, a tight stricture of the rectum was found, commencing 4 cms. above the anus. The mucous membrane was ulcerated, and had in great part disappeared. The thickness of the walls of the stricture was nearly one inch. The uterus and ovaries were normal, and were not involved in the rectal growth. The cæcum, with the ascending and transverse colon were greatly distended with flatus; the descending colon was rather small. The latter, together with the somewhat distended sigmoid flexure, contained putty-like fæces. The appendix vermiformis was six and a quarter inches long and free from adhesions. Its calibre was patent and contained no concretions. From the middle of the transverse colon to the stricture of the rectum the intestine was studded with polypi, about 170 in number in all —most numerous in the sigmoid flexure and in the rectum. Most were sessile, from 1 mm. to 1 cm. long, and from 1 mm. to 5 mm. broad. Others were pedunculated, from 5 mm. to 4 cms. long, and with a globular, raspberry-shaped mass at the end, from 1 cm. to 3 cms. in diameter. (These measurements were taken in the spirit preparation.) At the middle of the transverse colon there was a sessile polypus about the size of a small walnut. The base of it was infiltrating the intestinal wall, and had given rise to a puckered stricture which would admit one finger. The small intestine was normal. The mesenteric and lumbar glands were not much enlarged. The kidneys, right 4¾ ozs., left 5¼ ozs., contained no new growths, and were fairly healthy. The spleen weighed 9½ ozs., but was free from secondary growths. The liver weighed 7 lbs. 12 ozs., and contained several enormous masses of secondary growth and innumerable smaller ones. The gall-bladder was unaffected, small, and contained inspissated bile. There were no secondary growths in the lungs, but the bronchi of the lower lobe of the left lung were cylindrically dilated. The stomach and pancreas were healthy.

"On microscopic examination of the rectal stricture, the growth was found to involve chiefly the muscular coat. The peritoneal coat was unaffected. The mucous membrane, together with a portion of the submucous coat, had disappeared by ulceration. The growth was made up of irregular much-branched and indented spaces, lined with a *single* layer (never more) of cylindrical epithelium, united together by a slight richly cellular stroma. The sections were so extremely friable that they could only be held together by celloidin, in which accordingly all the specimens were embedded. The growth was what is often called a 'cylindrical epithelioma'; but, from the very evident way in which the gradual changes in structure could be traced in this case, from the simple adenoid polypus to the malignant growth with secondary deposits, I think it is better termed a 'malignant adenoma.' The secondary deposits in the liver were of the same nature as the rectal growth, but the spaces were much less regular, the cylindrical epithelium cells were scattered about in many parts in a very irregular way, and in some places there was a tendency towards an alveolar arrangement, just as in carcinoma, but this was nowhere well marked.

"The simple sessile polypi showed the usual arrangement of a central

connective tissue core containing the blood-vessels, and a somewhat thickened layer of mucous membrane covering it. The latter contained the ordinary tubular glands, but some of them had begun to widen out, enlarge, and become irregular.

"In the polypus associated with the stricture at the splenic flexure the transitional stages to a malignant growth could be well observed. The tubular glands had spread out into large, irregular cysts, or cavities lined with cylindrical epithelium, always in a single layer. In some places the epithelium lining these cysts had become folded and invaginated by the ingrowth of the richly cellular stroma. In other parts there was a completely irregular growth, in which cylindrical cells and round cells were mixed up in inextricable confusion, and were surrounded by an incomplete stroma. The structure of the malignant stricture of the rectum was perfectly indistinguishable from that of the polypus, except by the presence in the stroma of the muscular fibres of the intestinal wall.

"If there had been no secondary stricture, and had the structure of the rectal stricture not shown the remarkably close resemblance to that of the polypi, and finally, had not a polypus been found in the process of forming the splenic stricture, it might have been supposed that the rectal stricture was simply due to the long-continued mechanical irritation of the large polypus removed during life, just as the irritation of a tooth or a pipe-stem may determine the locality of an epithelioma of the tongue or the lip. But under the circumstances described, the connection between the polypi and the stricture was, in all probability, much closer."

CHAPTER IV

COMBINATION OF CHARACTERS

As already explained, this expression means the presence in certain otherwise innocent tumours of characters which are usually believed to belong only to malignant tumours.

The characters referred to depend upon the power of producing secondary deposits. This power of propagating new and separate foci of tumour growth is one of the most striking features of malignant tumours, and constitutes one of the many dangers to life which attend their growth. If we can show that some innocent tumours also possess this power of propagation, even although to a modified extent, we shall have given another reason for believing that the two kinds of tumour are essentially similar.

I.—The Contagious Properties of Simple Papilloma.

(1) *Warts on the Hand of a patient scraped off by medical attendant with his nail, followed shortly by growth of warts under that nail.*

This case was published by Dr. Payne in the *British Journal of Dermatology* for 1891, p. 185.

> "Charles B., æt. 11, healthy boy, out-patient in St. Thomas's Hospital, with a very copious eruption of warts. The right hand was nearly covered with them, chiefly the dorsal, but also the palmar surface. On the left hand they were rather less numerous. There were also a very large number of them on the face. The origin of the eruption was traced to a very large and horny wart on the palm of the right hand, which had existed more than two years. From this point the warts had spread over the right hand, then to the left, and had lately been extending very rapidly over the face. The total number must have been between two and three hundred. The boy was neat and cleanly for a child of his class, and his mother, a sensible, intelligent woman, gave a very clear history of the whole eruption. As the affection was very severe and disfiguring, I took a good deal of pains in treating it locally, and after trying various means, of which salicylic acid, collodion, and acetic acid were the most efficient, succeeded in completely removing the trouble. When the warts were rendered soft and crumbling by the methods adopted, I found the process was accelerated by scraping them away with the back or handle of a scalpel or similar instrument, and on one occasion thoughtlessly used my thumb-nail to assist the operation. The result convinced me once for all of the contagiousness of warts. After a few days I noticed some redness and swelling under the

thumb-nail which had been thus used, and in about a week an unmistakable horny wart appeared on the spot. Afterwards a second, and then a third, wart appeared on the back of the same thumb. I abstained from treating these in order to watch their development, but in a few weeks they all spontaneously disappeared. Not having suffered from anything of the kind either then, or, as far as I can remember, in my life, I cannot doubt that these little troubles were due to some contagious matter lodged under the thumb-nail, where it was not removed by the ordinary process of ablution."

II.—The Contagious Properties of Venereal Warts.

In 1896 I published a paper entitled "Venereal Warts a Contagious Form of Tumour" in the *Journal of Pathology and Bacteriology*, and discussed the subject at length.

The following are one or two of the cases upon which my view was founded, and I have seen no reason to change it since.

(1) Case 12.—*Warts round Anus, extending within sphincter; no illicit intercourse.*

"John R., æt. 29, married; was admitted to the Male Lock Ward in May 1895, to have warts round and within anus removed. He denied having had intercourse except with his wife, and had no sign or history of venereal disease of any kind. He said that for the last twelve years he had been aware of three small 'tumours' (warts) near his anus. They had remained unchanged until the beginning of the year, when they had begun to grow and multiply without apparent cause. The skin round the anus was quite covered with warts resembling those seen in venereal cases when, as often occurs in women, the warts spread from the genital organs to the anal region. When the patient was anæsthetized for the removal of the warts, I found that they had spread up the anal canal, and it was necessary to stretch the sphincter thoroughly before I could reach them. They must have extended quite to the top of the anal canal, *i.e.* that formerly known as the third part of the rectum."

(2) Case 1.—*Numerous Warts on the External Genitals of a young woman shortly after marriage; previous warts on the glans penis and prepuce of the husband.*

For this case, and for permission to publish it I am indebted to the kindness of Dr. Allan Jamieson.

"Some years ago Dr. Allan Jamieson was consulted by a recently married, thoroughly respectable young woman, with the following history. Not long after marriage she had felt discomfort about the vulva. This had increased, and on examination a few weeks later, Dr. Jamieson found the labia covered with a luxuriant crop of warts. He interviewed her husband, and found that he had several warts on the glans penis and prepuce, which, he admitted, had been there when he was married. Neither husband nor wife had gonorrhœa."

(3) Case 4.—*Warts on Glans Penis; no discharge.*

"James S., came from Methil, Fife, as an out-patient to the Male Lock Ward for advice. He stated that he had had intercourse several times within

the last few months with a mill girl, but with no one else, and that latterly these warts had begun to grow on his penis. He had a slight degree of hypospadias, so that the urethra opened on the under surface of the penis, about the usual position of the frenum, and the prepuce showed the imperfect development which always accompanies this condition. There were three or four small warts close together on the dorsal side of the corona glandis, *i.e.* at the point furthest from the urethral opening. There was no gonorrhœa, nor discharge or sore of any kind about the penis, and he said there never had been. His general health was excellent.

"The warts were situated on the part least likely to be affected by urethral irritation, had it existed."

(4) Case 6.—*Warts; no discharge; previous gonorrhœa without warts.*

"George M., came as an out-patient to the Male Lock Ward on the 9th of May 1895. He had had frequent intercourse from time to time, and several attacks of gonorrhœa. About three weeks after he had got rid of his last attack of gonorrhœa, he had connection again. Not long after this he felt discomfort under the prepuce, and soon the warts appeared for which he sought advice. He had a number of small warts on the prepuce and glans penis, but no urethral discharge, and no balanitis."

"The special importance of this case is that gonorrhœa failed to cause warts to grow in a patient whose liability to their development was subsequently proved by their appearance after connection, but without apparent irritation."

(5) Case 8.—*Extensive development of Warts on the vulva; no gonorrhœa or other vaginal discharge.*

"This patient, C. B., a previously respectable girl from a town in Fife, asserted that she had been seduced by her sweetheart. On her admission to the Female Lock Ward, a very extensive growth of warts which had followed her seduction completely covered her labia on both sides. There was considerable foul-smelling discharge from the warts. Under chloroform, the warts were clipped away with scissors, and during the operation I examined the vagina, and was struck by its entire freedom from discharge. She made a good and quick recovery, and had no vaginal discharge from first to last."

III.—Contagious Property of Innocent Tumours within the Peritoneal Cavity.

If the conditions present on the outer surface of the body permit certain innocent tumours to display a power of dissemination by local infection or contagion, still more should the conditions found within the peritoneal cavity permit tumours in that region to manifest any contagious property which they may possess. On the outside of the body the cuticle on the exposed parts offers a firm, dry barrier against the entrance of any living cell. Moreover, washing and rubbing against surrounding objects tend to remove any such living cells, even although under favourable circumstances

they might have penetrated the barrier. Only, therefore, when the cuticle has been abraded, cracked, or softened, and when also washing has been neglected, could living cells laid on the surface of the skin show that they were capable of developing into a tumour. Within the peritoneal cavity, however, the conditions are much more favourable. The surfaces are always moist, the protective endothelial barrier is extremely delicate, the temperature is uniformly that of the blood, and there is no mechanical agent to remove a living cell if it should lodge on the surface of the peritoneum.

When these considerations are taken into account, it is not surprising to find that innocent tumours of the ovary are sometimes disseminated, owing to the setting free of their cells in the peritoneal cavity. This may be possible from the rupture of a cyst, from the projection of a papilloma into the peritoneal cavity, or from the escape of cells from a tumour in the course of an operation.

There is an advantage in taking the most definite cases first, for they render more credible other cases which, although similar, are not in themselves so convincing. For this reason we take first—

(*a*) *Innocent Papilloma bearing Cysts of the Ovary which disseminate Warts over the peritoneal surface.*

Mr. Bland Sutton (on *Tumours*, 3rd ed., 1903, p. 468), when speaking of cysts of the paroophoron, says: "It has been clearly established that, when the abdomen has been opened for the removal of a papillomatous cyst, the peritoneum has been found studded with warts. A few years later the abdomen has been reopened and all the abdominal warts have disappeared. They behave like warts on the skin. This fact must be borne in mind, or the operator will hastily assume the disease to be malignant when he finds general peritoneal infection. The disappearance of peritoneal warts after removal of the primary tumour is an interesting fact, and may probably be explained in this way. The life of multiple warts is often very transient, and this is probably the case with peritoneal papillomata; but as long as the seed-supply continues, new warts spring up, last for a time, and die, to be succeeded in their turn by a new crop. When the source of epithelium is removed by operation, the warts then existing die, and the crop of warts is not renewed. Exceptionally, these papillomatous cysts rupture into the connective tissue of the mesometrium, and I have seen them clustering around the urachus as high as the umbilicus."

Among many published cases of the kind referred to in these remarks, the following may be taken as a good example. It is one of a series of "Papilloma bearing Ovarian Cysts," published by the late Mr. Knowsley Thornton in the *Medical Times and Gazette* in June 1881:—

Case 6.—*Rupture of Cyst, with infection of peritoneum. Successful ovariotomy; followed by pregnancy.*

"A. M. K., married four years, and mother of two children, consulted me in January 1877. She had been gradually enlarging since the birth of her youngest child two years before, and I found a large free ovarian cyst, but could not persuade her to have it removed. She returned home, and very shortly afterwards began to decrease in size, the decrease being accompanied by

abdominal tenderness and profuse diuresis. In the following January she returned as large as before, and I performed ovariotomy. The whole pelvic peritoneum was covered with a small hard papilloma, and I could not accurately distinguish the left ovary, but felt something like it covered with papilloma, and bound down by adhesions, at the bottom of the pouch of Douglas. The tumour was made up of one thick-walled cyst lined with papilloma and a number of smaller cysts grouped about its base, and all of these which I opened contained similar papilloma. A large patch of the main cyst wall was white, sodden, and non-vascular, and in the centre of this patch there was a round hole of the size of a shilling. The patient made a rapid recovery, but the thickened condition of the broad ligament, and partial fixing of uterus when she left the hospital made me fear to hear of some recurrence. Instead of this, however, I am happy to report that she is in good health and has had a fine boy since the operation—the period of gestation and the labour being in every respect natural."

Remarks.—"Case 6 was an example of the recurrence of the small, hard, warty papilloma in a multilocular cyst and in all its cavities. This is comparatively rare, and, together with the rapid infection of the peritoneum with the rupture of the cyst caused me to form a bad prognosis; but three and a half years have passed and the patient is in perfect health, and is the mother of a fine healthy boy, so that I begin to take a more favourable view of her case, as the pregnant condition seems to me especially prone to hasten existing, or bring out latent, malignant disease."

There can be no doubt that some of these cases are truly malignant, and Thornton describes one such. We need not, however, go into that question here, as it has been dealt with in Chapter I. At present we are concerned with innocent tumours.

(*b*) *Innocent Pseudomucinous Papillary Adenoma, causing Secondary Growths of a similar kind on the adjacent peritoneal surface.*

Professor Howard Kelly (*Operative Gynæcology*, 1898, vol. ii. p. 272), referring to this class of tumour, makes the following remarks:—

"This group of papillary tumours resembles in external appearance the classical polycystic ovarian cysts, and really belongs to the same class." . . . "The pseudomucin is a dark secretion from the epithelial cells, and not a form of degeneration. The growth of these tumours is slow, and not accompanied by marked discomforts; indeed, their tendency is throughout benign; in marked contrast to the papillary adenomata of the next group with ciliated epithelium, and to the papillary carcinomata. In seven cases, implantations on the peritoneum were found but once, in spite of the presence of papillary excrescences on the surface of the tumour in a number of instances. In the cases in which the implantations were found, they appeared as little glassy nodules, which were not papillary, but resembled those found with the ordinary ovarian cystomata."

(*c*) *Innocent Glandular Ovarian Cysts, causing similar implantation Cysts on the surface of the Peritoneum.*

The last sentence quoted from Kelly evidently refers to this form of infection. That author does not make any further allusion to the subject,

although he speaks as if the occurrence of such implantation cysts was well known.

In Professor Pozzi's *Treatise of Gynæcology*, English translation, 1892, vol. ii. p. 118, the following passage occurs :—

" Metastatic infection of the peritoneum has been very rarely observed in glandular ovarian cysts. It seems to follow spontaneous rupture of the cyst, and we often find in the peritoneal cavity small sacs, with or without accompanying gelatinous masses, grafted upon the epiploon, on the intestines, or retroperitoneal. I recently saw a case of this kind. The tumour was bilateral, polycystic, and there were metastatic growths in Douglas cul-de-sac, besides the free cyst of the size of an orange which adhered to the intestines, and doubtless came from the rupture of one of the ovarian tumours; there was slight ascites; the patient succumbed rapidly. Runge, in a similar case (" Fall von glandulären ovarial cystomen mit gelatinosen inhalt und peritonealen Metastasen "—*Centr. f. Gynäk.*, 1888, No. 15), obtained a complete cure six months later. Cystic growths were scattered upon the epiploon, bladder, and posterior abdominal wall."

Dr. R. Olshausen has published a paper on this subject under the title of " Metastasen-bildungen bei gutartigen ovarial Kystomen—Metastatic Formations in Innocent Ovarian Cysts " (*Zeitschr. f. Geburt. und Gynäk.* ii. p. 238). After some introductory remarks, he narrates the details of the case on which his paper is founded, and makes the following summary of it :— " Therefore, after complete extirpation of a degenerated ovary—proliferating cystoma—and after an easy, clean operation, during which only very little at most of the contents of the tumour were left in the abdomen, there was formed in the course of two years a tumour, 7 lbs. in weight, in the cavity of the pelvis, which did not arise either from the other ovary, which was sound, or from the stump of the pedicle. The tumour contained the same kind of tough jelly that had been present in the tumour we removed before. Throughout this jelly there were a number of thin membranes, supplied with the same epithelium as is always seen in ovarian cystoma. What, I ask, can be inferred under these circumstances, except that this tumour has arisen from the growth in the cavity of the peritoneum of small particles of the ovarian tumour ? Whether we call this metastasis or peritoneal return is of no importance. It would be idle also to discuss whether this tumour was deposited in the cavity of the peritoneum while the ovarian tumour was present, perhaps from its bursting and so allowing particles to become free ; or whether such particles were left at the operation, and only afterwards began to grow. If the latter is possible, the former is also conceivable."

As some of the details of the description of the tumour are important for our present purpose, they may be quoted in addition to the preceding summary.

" On opening the peritoneal cavity, not only were masses of jelly found, but between the masses there were numerous thin membranes, which could be easily burst by a little pressure of the finger, the point of the finger then could be felt to enter distinct compartments. Professor Ackerman, who examined these fine membranes under the microscope, found that they were

composed of delicate connective tissue, and that their surfaces, which were turned towards the jelly, were covered with small cylindrical epithelial cells with a large nucleus. Similar cells, only less definitely cylindrical, and at great intervals from one another, were found scattered in the interior of the free masses of jelly. Professor Ackerman, at the end of his report, uses the expression, 'Metastases from ovarian cystoma.'"

(*d*) *Dermoid Cysts of the Ovary—presumably innocent—which have caused the growth of similar Cysts on the surface of the Peritoneum.*

Fränkel, in 1883, published a paper (*Wiener. med. Wochen.*, 1883, p. 865) with the title of "Dermoid Cysts of the Ovaries, and at the same time Dermoids in the Peritoneum." The cases which gave occasion for the paper are narrated in full: some of the more important details are as follows:—

(1) *Dermoid Cyst of the left ovary; multiple dermoids in the peritoneum; cystovariotomy; peritonitis; death.*

"Married woman, æt. 37. Had had four normal childbirths, the first thirteen years before admission to the hospital; the fourth, eight years before; also an abortion, five years before, following an injury. Two years before she came under observation she had a sudden attack of retention of urine. The medical attendant who was called in recognized a tumour about the size of an apple in the right iliac fossa. This gradually increased, and could be felt also on the left side of the pelvis. Nine months before admission to the hospital she had fallen on her back from a tram-car, and for three weeks afterwards had been confined to bed with severe pains in the abdomen and small of the back, accompanied at first by feverish symptoms.

"When she applied for advice, her chief symptoms were a feeling of great weight in the abdomen, shortness of breath on exertion, with occasional pain in the small of the back. Operation was performed the 9th of December 1882. When the peritoneal cavity was opened there were evacuated 5 litres of turbid, yellowish-green fluid, with fat and cholesterine floating on the surface, and a mass of matted hair and caseous material. A dermoid cyst of the left ovary was recognized, and in spite of every care, some of the dirty yellow fluid contents, mingled with fat, cholesterine, and hairs, escaped into the peritoneal cavity. The cyst was enucleated only after considerable trouble, owing to its adhesions. Numerous small dermoid tumours filled with hair and caseous material were attached to the omentum. Others, more cystic in nature, and varying from the size of a walnut downwards, hung by slender stalks into the peritoneal cavity. Others were found in the interior of adhesions. Many hairs also projected freely from the surface of the omentum. The patient died next day, with symptoms of acute septic peritonitis.

"At the post-mortem examination, numerous dermoid cysts, varying from the size of a hemp-seed to that of a pigeon's egg, were scattered over the whole of the peritoneal cavity.

"The interior of the main cyst was found to be mamillated all over, and the surface was in some places like epidermis, in others like mucous membrane.

(2) Fränkel's second case was that of a woman, æt. 41, who had had an abdominal tumour for fifteen years. At the operation, a dermoid cyst of the right ovary was found, with similar growths on the mesentery. During the operation, which was a very difficult one, the intestine was torn, and the patient

died of septic peritonitis two days afterwards. At the post-mortem examination, numerous dermoid cysts with honeylike contents, and varying from the size of a hemp-seed to that of a hazel-nut, were found attached to the peritoneal surface of the intestines; one had atheromatous matter in the interior; the others contained a honeylike fluid.

A phenomenon similar to the preceding, but even more remarkable, is the following:—

IV.—The Development of a Malignant Tumour in an Abdominal Wound made for the removal of an Apparently Innocent Tumour of the Ovary.

Professor Pfannenstiel ("Carcinomabildung," *Zeitsch. f. Geburtsch. und Gynäk.*, Bd. xxviii. S. 361 ff., 1894) gives an abstract of eleven cases in which cancer developed in the scar of a wound made for the removal of a tumour of the ovary, believed at the time of its removal to be innocent. As, however, in most of these cases no exact examination of the structure of the primary tumour had been recorded, he thought it important to publish a case of the sort in which there had been a careful macroscopic and microscopic examination of both the primary and the secondary tumour.

A married woman, æt. 30, was operated on in January 1889 on account of a tumour of the ovary. When the peritoneal cavity was opened it was found to contain a quantity of thick, turbid, yellow fluid, which was somewhat sticky. The tumour was incised, but as very little fluid escaped on account of its being so thick, the wound was enlarged and the operation completed without reducing the size of the tumour. There was a well-formed pedicle about the thickness of three fingers, which was ligatured and divided. The patient made a good recovery, and remained quite well for a year or two. Then (but the exact date was not known) a swelling appeared at the lower end of the scar. This extended downwards and to the right, and was accompanied by pain in the groin and thigh, and right side of the pelvis.

In January 1893 the patient was examined, and was found to be suffering from a growth in the lower end of the abdominal scar, which had invaded the abdominal wall, and had caused glandular enlargement in the right groin and iliac fossa. This growth ulcerated, and the patient grew weaker, and died in June of the same year, *i.e.* about four and a half years after the operation.

At the post-mortem examination the immediate cause of death was found to be bronchopneumonia. The stump of the pedicle was quite healthy. The remaining ovary contained a small cyst, but was otherwise healthy. There were no secondary deposits in the lungs or other viscera. It was evident that the infiltrating new growth of the abdominal wall had begun in the scar of the former operation, and had caused the involvement of glands in the right groin and iliac fossa.

The original tumour and return growth in the scar were carefully examined, and illustrations of the microscopical structure of both are published with the paper. The original tumour was a "Kystadenoma ovarii pseudo-mucinosum," of the innocent character of which there seemed to be no doubt. Pfannenstiel is quite sure it was not a mixed tumour. The tumour in the scar had a twofold character. In some places its structure was practically the same

as that of the original tumour, while in other places it had the structure of a well-marked adenocarcinoma. Pfannenstiel believes that the secondary tumour in the scar was at first innocent, and afterwards became transformed into cancer.

The mucoid contents of the cysts in the secondary deposit were quite similar to those in the primary growth, and this, together with the close resemblance of the two growths under the microscope, makes it certain that this was a case of implantation in the wound of material derived from the primary tumour when it was punctured during the operation, in the hope of reducing its size. In other words, a cystic tumour of the ovary which was indistinguishable from an innocent tumour of that organ, and which, after removal, did not return at the original seat, yet returned in a malignant form in the scar of the abdominal wound, that wound having been bathed with the contents of the cyst during the operation.

The foregoing instances seem to warrant us in asserting—(1) That certain innocent tumours may give rise to secondary deposits of innocent tumour growth of the same kind, when circumstances permit particles of the original tumour to be transplanted to adjacent parts of the body, and allowed to rest there until they have had time to develop; (2) That under similar circumstances certain innocent tumours may even give rise to secondary deposits of malignant growth. We have already seen that innocent tumours may become transformed into malignant tumours of the same type of growth; from this it is only a step to the transformation taking place in the secondary deposits instead of in the original tumour. Moreover, in malignant tumours the secondary deposits are often, if not generally, more actively malignant than the tumour from which they arose. The primary focus may indeed be so small and so slow of growth that it may escape notice, while the secondary deposits may assume malignant characters of the most active and severe type. Every clinician of experience is familiar with this phenomenon, and its occurrence renders the much rarer phenomenon of secondary malignant deposits arising from primary innocent growths more easy to understand.

In medical literature, however, there have been published instances where innocent tumours have shown their power to give rise to secondary growths, not by means of particles set free in a cavity or on the surface of a wound, but through the blood-stream. This need not surprise us. If innocent tumours can be disseminated by portions of their substance becoming free in the peritoneal cavity, or in wounds, why not by such portions becoming free in the blood-stream? Probably this latter form of dissemination so seldom takes place, only because innocent tumours so seldom set free any of their cells into blood- or lymph-stream. If they could more readily do so, we might expect secondary growths to result from them more frequently. To judge from what we have seen innocent tumours to be capable of in the peritoneal cavity, we might expect secondary deposits, carried from innocent tumours by the blood, to be generally innocent in character but sometimes also to be malignant. As a matter of fact, instances of both forms of secondary deposit have been recorded in medical literature.

V.—Innocent Tumour giving rise to Secondary Deposits (Innocent or Malignant) through the Blood-stream.

Dr. Ludvig Pick, in 1897, published a paper in the *Berliner klin. Wochenschrift* upon what he entitles, "Hydatid Moles which form Innocent and Malignant Metastatic Deposits" ("von der Gut und bösartig metastasirenden Blasen mole").

The paper was upon the following case:—

> "A woman, in the fourth month of pregnancy, was admitted to the clinique of Professor Landau on account of flooding. A small tumour about the size of a walnut was found growing on the wall of the vagina, and was excised on the 2nd of May 1894. This, on microscopic examination, proved to be a true vesicular chorionic growth. Two days afterwards there was considerable metrorrhagia, and on the 25th of May a vesicular mole was passed. The patient made a complete recovery, and on the 19th of November 1897 was delivered of a healthy baby (girl) at full time."

Pick, on the strength of this and similar cases, believes that innocent vesicular moles may give rise in the vagina to embolic metastases which consist of a nucleus of chorion villi with a covering of clotted blood.

The *Thyroid gland* is another part of the body where innocent tumours have given rise to metastatic deposits in distant parts. Many independent observations of this phenomenon have been published. Among others, M. Patel, in the *Revue de Chirurgie* for 1904, has published an interesting case and referred to eighteen others which had been published previously. The title of his paper is "Innocent Tumours of the Thyroid which caused Metastatic Deposits" ("Tumeurs benignes du Corps Thyroide donnant des Metastases"). The metastases were most frequently found in the bones, especially the cranium, lower jaw, vertebral column, pelvis, and long bones. The lungs were also frequently affected, but in them the deposits were generally small and unaccompanied by clinical symptoms.

The Nature of the Metastases.—From a histological point of view these were in some cases considered to be innocent and in others malignant.

The *symptoms in the thyroid gland* itself were generally conspicuous by their absence. In some cases the thyroid *seemed* quite normal; in some, goitre had been present for many years, but had remained unchanged. In others, there might have been a slight enlargement of an old-standing goitre, but even then there had been nothing to suggest a cancer of the thyroid.

The symptoms *produced by the metastases* varied according to the position of the deposit, the direction of its growth, and the parts which it pressed upon. Often, the external swelling was the first symptom observed.

The following, quoted by Patel from Kraske, is an example of an innocent thyroid tumour with an innocent metastasis:—

Innocent Goitre with Cranial Metastasis (Obs. v., abstract, Kraske's personal observation).

> "Woman, æt. 53, affected with swelling of the body of the thyroid. Secondary tumour, solid, and indolent, on the frontal bone. According to the patient's account, this tumour had grown in the space of six weeks, and had followed a blow.

"At the operation it was found that the tumour, originating in the diplöe, had perforated the skull both inwards and outwards. On account of the hæmorrhage, the tumour was removed in two stages. At the end of three years there was no return.

"Under the microscope, the structure of the frontal tumour was found to be analogous to that of the thyroid gland but of a larger size ('d'une structure analogue à celle de la glande thyroide dont le volume est augmenté')."

The patient, whose case was observed by M. Patel, had been under the care of Professor Jaboulay.

Innocent Goitre with Malignant Thyroid Metastasis at the internal orbital angle of the left frontal bone.

Marie G., æt. 65, was admitted to Professor Jaboulay's wards on the 13th of October 1902. There was nothing of importance in the family history or patient's previous health. She had a hypertrophied thyroid gland which had remained without apparent change for thirty years. Three years before admission she had had an accident, the nature of which was not stated. Four months before admission the symptoms had begun (presumably by pain, but this is not stated). She had been unable to continue her work as a dressmaker, from inability to keep her attention fixed upon the work. Some days afterwards the swelling appeared at the inner angle of the orbit, extending to the root of the nose and region of the eyebrow at the left side. This swelling varied in size and was tender to the touch. The upper eyelid moved freely, and there was no protrusion of the eye, but the frontal sinus seemed to be pushed forward. Six days later there was some epistaxis.

The long-standing enlargement of the thyroid gland had not only not increased latterly, but in fact had become smaller within the last two years. It was free from any physical or functional sign of malignancy ("sans signes physiques ni functionelles de malignité"). In contrast with the thyroid swelling, the progress of the swelling at the inner angle of the orbit had been rapid, and accompanied by pain. It pulsated, and moved every way with each beat of the pulse. Large vessels covered the surface. The nasal cavity had required to be packed twice, on account of the epistaxis. Operation—on exposing the tumour and raising it up from its bed, the frontal bone was found to be eroded, and the dura mater which was then exposed, was seen to pulsate. The pulsation of the tumour had been due to its resting against the pulsating dura mater. The tumour was removed, and the edges of the gap in the skull were taken away in case they might have been invaded by the tumour. The wound was packed, and healed satisfactorily.

The result of the microscopic examination is summed up as follows: The tumour was of the type of the thyroid. Certain parts reproduced exactly normal thyroid tissue, while other parts had the character of a highly malignant epithelioma.

In October 1903 the patient was found to be suffering from a return of the growth at the seat of the operation, with much epistaxis. Her general health was much impaired, and death was imminent. The thyroid swelling had not increased in size.

This is an example of an innocent thyroid tumour with a malignant metastasis.

CHAPTER V

CONCLUSION AND DEDUCTIONS

THE three important features of tumour growth which were mentioned at the outset of this treatise have now been illustrated. We have seen, on the evidence of many independent observers, that no hard and fast line of demarcation can be drawn between the innocent and the malignant representatives of many different types of tumour; that the same tumour may be at one time innocent, at another time malignant; and that the power of dissemination, instead of being limited to malignant tumours as was formerly supposed, is possessed also by many innocent tumours. I do not see how to explain these facts on any other basis than that innocent and malignant tumours are essentially similar; in other words, that they are similar to one another in their nature and mode of growth, whatever that may be. Other minds considering the same evidence may not come to the same conclusion, but in that case more evidence of the same kind would not be likely to convince them. The deductions which follow from the conclusion that innocent and malignant tumours are essentially similar are of very great importance, and may be stated as follows:

1. No theory of the *causation* of tumour growth can be satisfactory which does not apply equally to innocent and to malignant tumours.

A large number, if not the majority, of the investigations recently undertaken to try to discover the cause of Cancer have been based on the assumption that Cancer is a disease by itself. Typical examples of malignant disease have been selected, and all reasoning has been based upon them. The parasitic theory of the cause of Cancer is a good example of one founded on this assumption; but there are many others.

While, of course, useful knowledge has often been brought to light from investigations founded upon a false theory, it is also true that a false theory has frequently led to much misapplication of energy and to corresponding waste of time. Even although the essential similarity view may be a very general one, it will help us in our investigations if it does nothing else than keep us from following paths along which we shall have afterwards to retrace our steps.

2. No search for a *cure* for Cancer is likely to be successful (unless by chance) so long as the search is directed by the theory that Cancer is a disease by itself. It must be admitted that many valuable remedies for disease have been discovered in the past by chance; sometimes when no

search was being made at all, sometimes during a search based on an erroneous theory. Still, it is surely more economical of time and energy if, when seeking a remedy for Cancer, we can have certain limits defined for us within which the path to success must lie.

3. No type of tumour can be considered, with respect to *operative treatment*, to be necessarily exempt from the taint of malignancy. In other words, every innocent tumour has relatives of the same type, but which are, some more, some less, malignant. The surgeon who recognizes this will be saved from two extremes when he is dealing with semi-malignant tumours. He will not treat them too mildly, merely because innocent characters are recognizable, nor will he use extreme measures for removal as soon as the possibility of malignancy is suspected. He will, in fact, never be off his guard, and will try to weigh each case separately, and treat the tumour according to its nature and tendencies, although always inclining to early rather than to late operations, and towards removing too much rather than too little where there is room for doubt.

4. Most of the existing *statistics* indicating the relative malignancy of various kinds of tumour will have to be recast. Hitherto such statistics have been drawn up on the assumption that tumours are either innocent or malignant. No allowance has been made for tumours of intermediate grades of malignancy. If, however, any just comparison is to be made, the groups to be compared with one another must be composed of individuals similar as regards their degree of malignancy. Thus, if we wish to compare the malignancy of central and of periosteal sarcomata of bone, we must be sure that individuals composing each group belong to the same—say, the extreme —degree of malignancy. When this has been done, we might find, for example, either that the extreme degree of malignancy in each case was different, or that a similar degree of malignancy was reached in each case, although it might be reached more frequently in the one group than in the other. As a matter of fact, the latter alternative is what seems to be the usual one. Thus, for instance, the most terribly malignant forms of sarcoma may be found arising from the medulla no less than from the periosteum. Whether tumours endued with the same degree of malignant power arise more frequently in the periosteum or in the medulla is still uncertain, because apparently no one has as yet tried to compile statistics on this basis.

5. The quality of malignancy should be employed as a basis in the *Classification* of tumours. In the practice of medicine and surgery, the malignancy, or relative malignancy, of any tumour is vastly more important than its minute structure, except in so far as the structure may itself indicate the probable clinical character of the tumour. In subdividing, therefore, the larger groups of tumour framed upon a structural basis, it would be better to employ clinical instead of histological characters as the basis for that subdivision. In this way, the larger groups of new growths would consist of those individuals which had arisen from the same organ or tissue, and whose structure bore a traceable resemblance to one another, and generally also to that of the part in which they had arisen. Within each group thus formed the individuals would be arranged in the order of their clinical character, beginning with innocent and ending with malignant forms.

This method of classification is equally applicable to museum catalogues, or to text-books of pathology, medicine, or surgery.

Of course there are histological and naked-eye characters which correspond more or less closely to the variations in clinical character of the individual new growths. There is no need to ignore these structural characters. All that is urged is that the clinical should be considered of greater importance than the structural characters in the subdivision of the larger groups.

The three series illustrating gradation in malignancy in Chapter I. may be taken as examples of this method of classification applied to tumours of bone. Other examples may be found in the catalogue of the Museum of the Royal College of Surgeons of Edinburgh, where the same system has been applied to the tumours arising in other tissues and in the various organs of the body.

This method of classification has difficulties, in common with every other method; but it has the great advantage of arranging the student's knowledge in accordance with the facts brought under his notice in clinical work, while it is easily understood and easily remembered.

6. Much of the confusing *differences of opinion* held by different authorities as to the malignancy or otherwise of different kinds of tumour will be explained and reconciled. For example, myeloid tumours of bone were at one time considered to be always malignant; then the pendulum swung back, and many authorities considered them to be always innocent. The truth lies between these two extremes: myeloid tumours may be either innocent *or* malignant, *or* only partially so. The same may be said of every other recognized type of tumour.

FIRST GRADATION SERIES

Fig. 1.- Innocent Chondroma (No. 1)

Fig. 2.- Innocent Chondroma—Ossified (No. 2)

FIRST GRADATION SERIES—*Continued*

Fig. 3.—Large Innocent Chondroma (No. 3)

Fig. 4.—Patient after removal of Large Innocent Chondroma (No. 3)

Fig. 5.—Large Innocent Chondroma (No. 3)

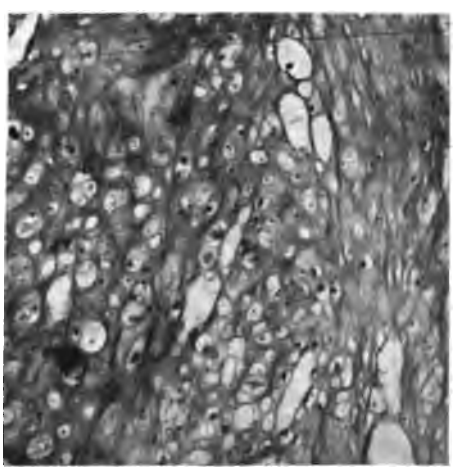


Fig. 6.—Photomicrograph of (No. 3)

FIRST GRADATION SERIES—*Continued*

Fig. 7.—Large Innocent Chondroma (No. 3)

FIRST GRADATION SERIES—*Continued*

Fig. 8. -Chondroma of Humerus (No. 4)

Fig 9.—Wax Cast of Chondroma of Humerus (No. 4)

FIRST GRADATION SERIES—*Continued*

Fig. 10.—Chondromyxoma of Thumb (No. 5)

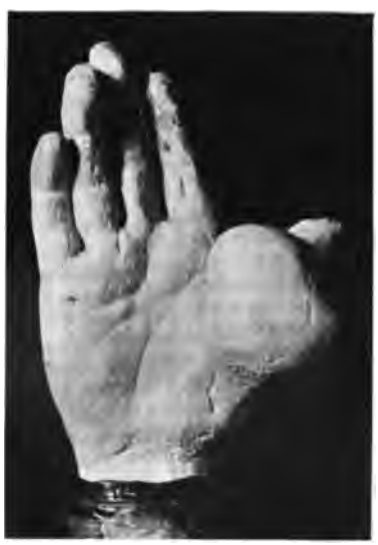


Fig. 11.—Chondromyxoma of Thumb (No. 5)

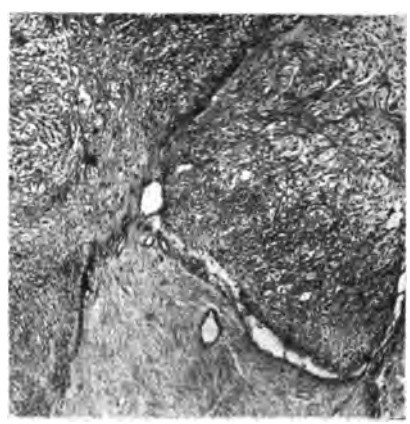


Fig. 12.—Photomicrograph of (No. 5)

FIRST GRADATION SERIES—*Continued*

Fig. 13.—Enormous Chondroma of Sternum (No. 6)

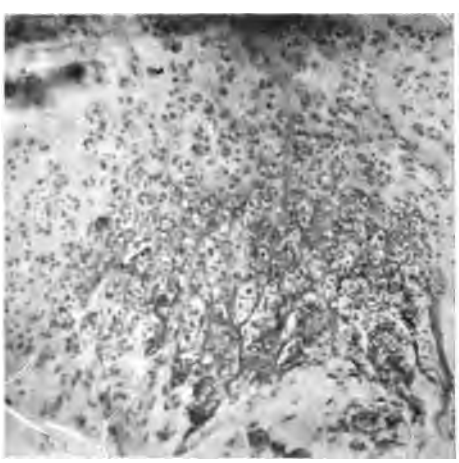


Fig. 14. –Photomicrograph of (No. 6)

FIRST GRADATION SERIES—*Continued*

Fig. 15.—Enormous Chondrosarcoma of Ilium (No. 7

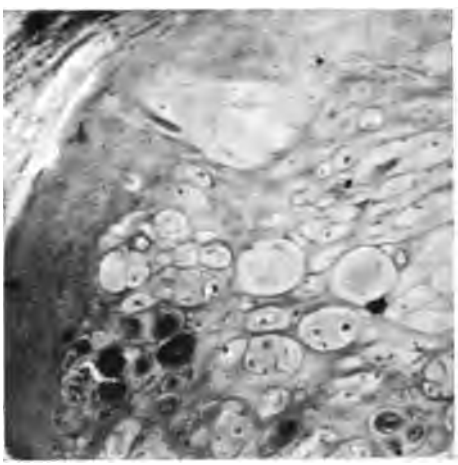


Fig. 16.—Photomicrograph of (No. 7)

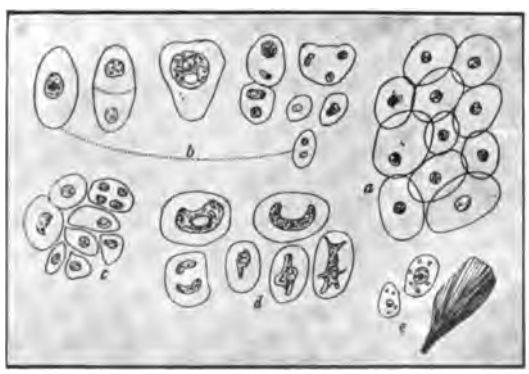


Fig. 17.—Drawing of Cells seen in (No. 7)
From St. Bartholomew's Hospital Reports, Vol. vi.

FIRST GRADATION SERIES—*Continued*

Fig. 18.—Enormous Chondrosarcoma of Humerus (No. 8)

Fig. 19.—Cast of (No. 8).

FIRST GRADATION SERIES—*Continued*

Fig. 20.—Part of Enormous Chondrosarcoma of Humerus (No. 8)

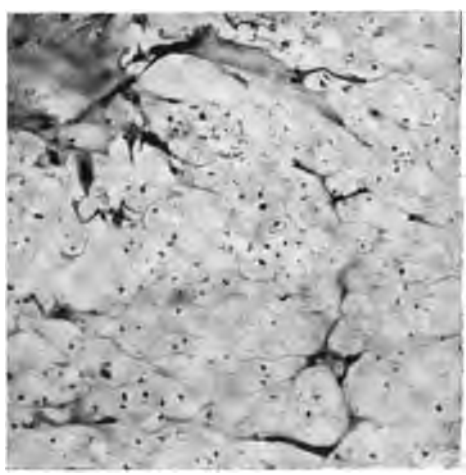


Fig. 21.—Photomicrograph of (No. 8)

FIRST GRADATION SERIES—*Continued*

Fig. 22. -Recurrent Chondroma of Humerus (No. 9)

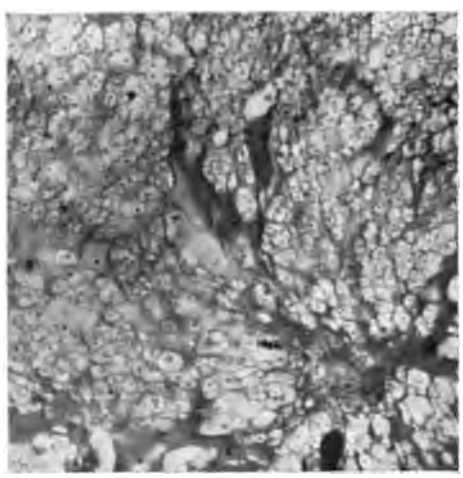


Fig. 23.—Photomicrograph of (No. 9)

FIRST GRADATION SERIES –*Continued*

Fig. 24.—Chondrosarcoma of Scapula (No. 10)

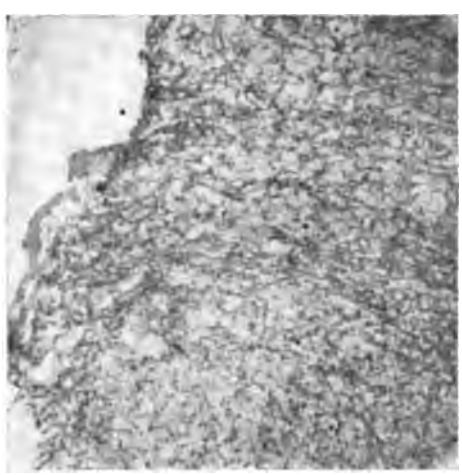


Fig. 25.—Photomicrograph of (No. 10)

FIRST GRADATION SERIES—*Continued*

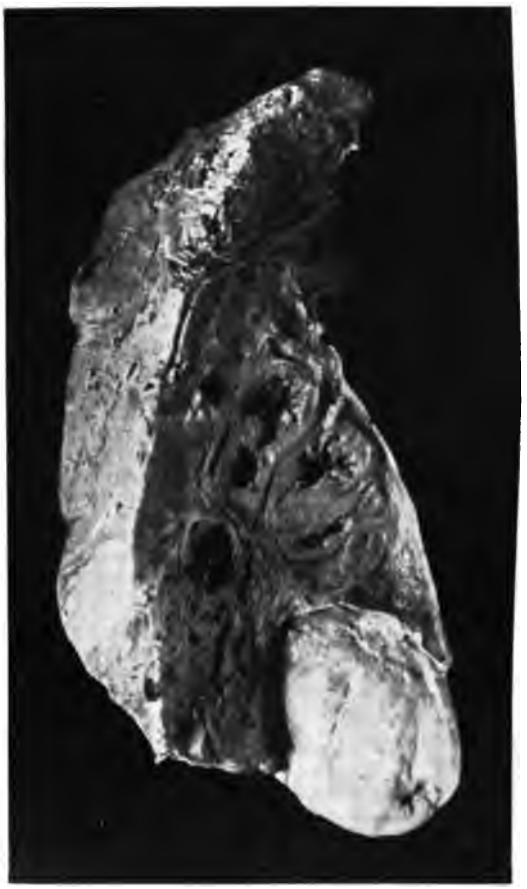


Fig. 26.— Metastatic deposits in Lung in Case (No. 10)

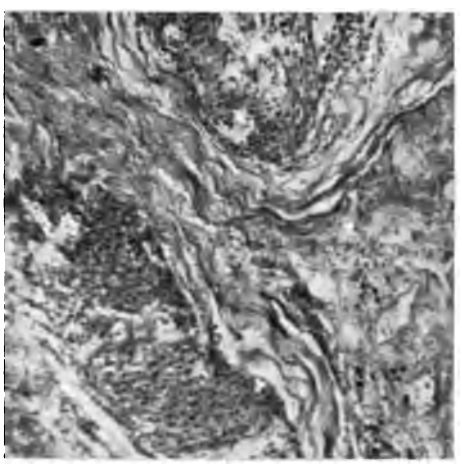


Fig. 27. - Photomicrograph of Metastatic deposit in Lung in Case (No. 10)

SECOND GRADATION SERIES

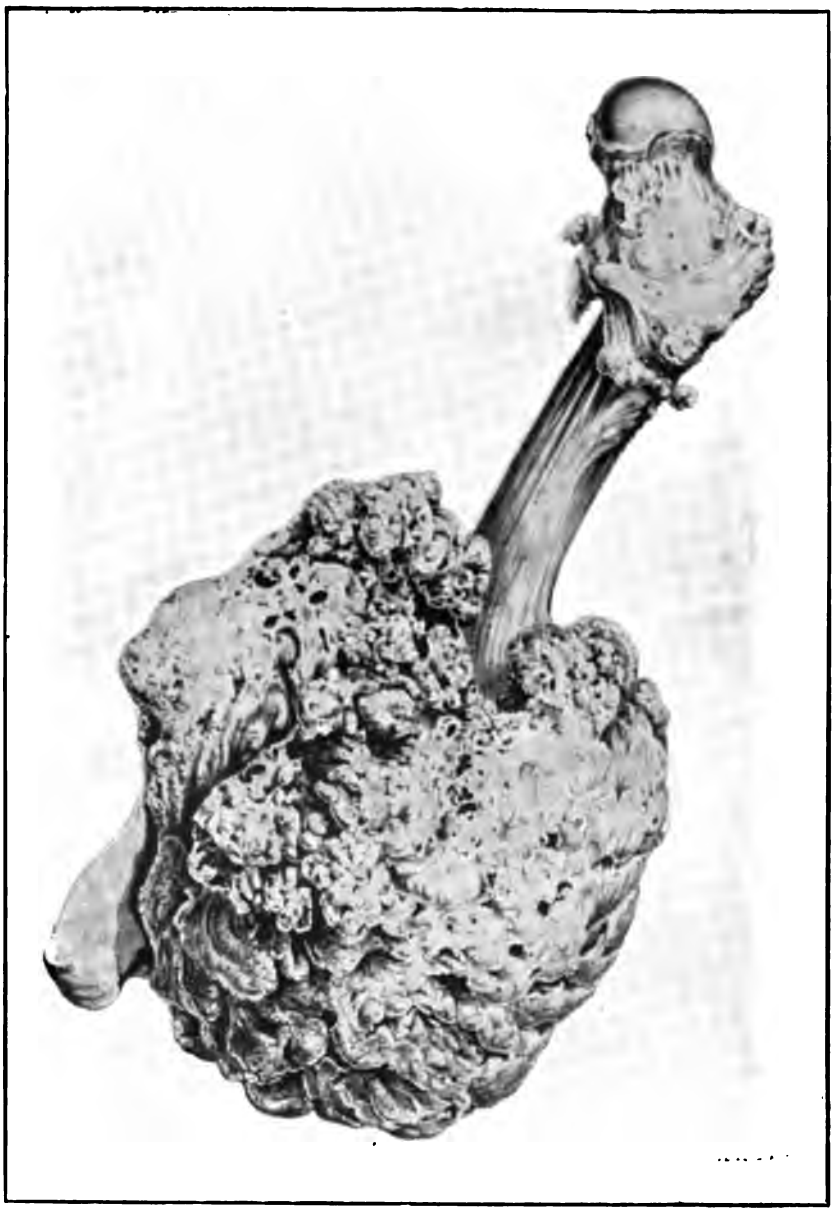
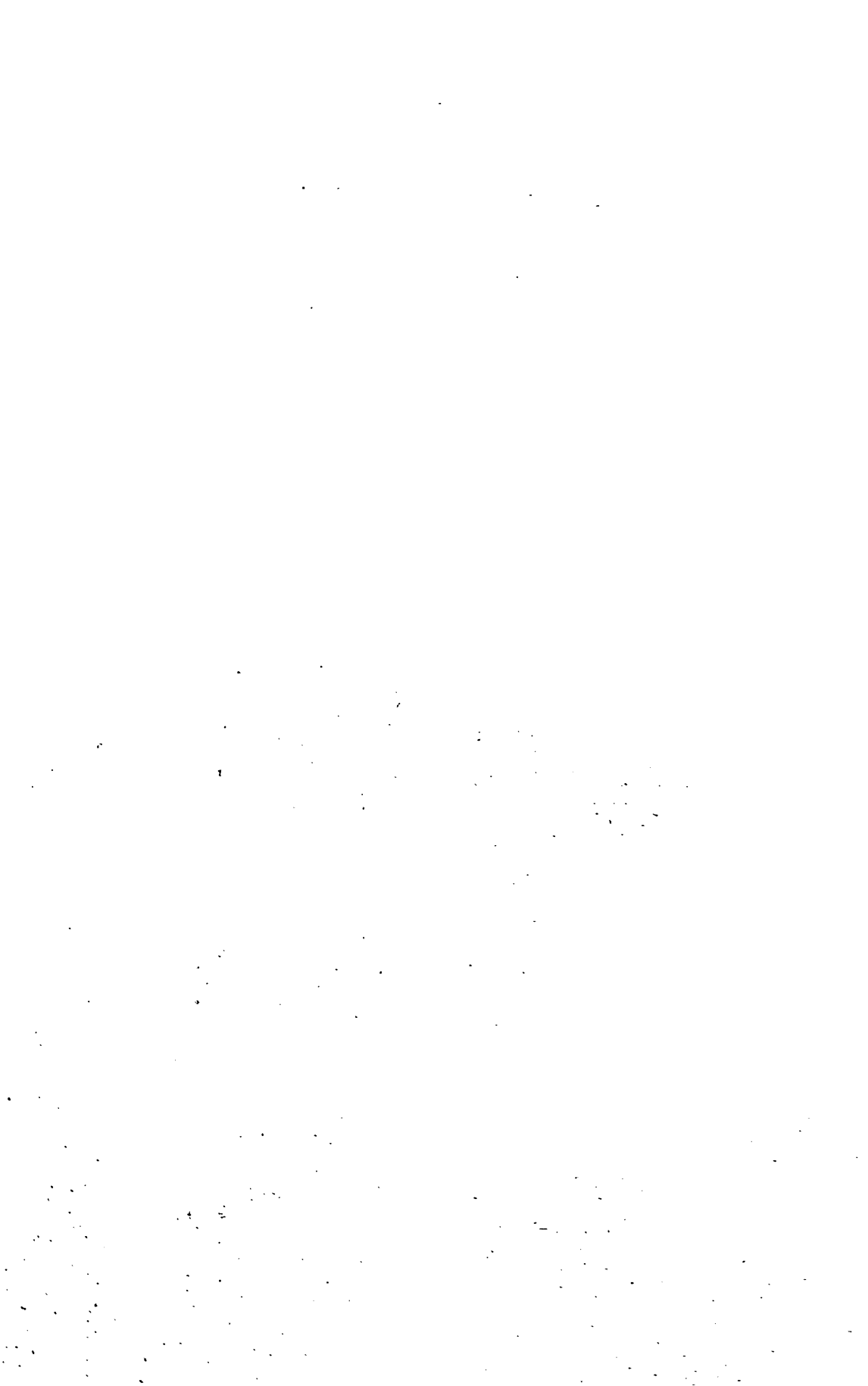


Fig. 28.—Innocent Osteoma of Femur (No. 1)



SECOND GRADATION SERIES—*Continued*

Fig. 29. -Innocent Osteoma of Humerus (No. 2)

Fig. 30. —Innocent Osteoma of Humerus (No. 2)
Back view

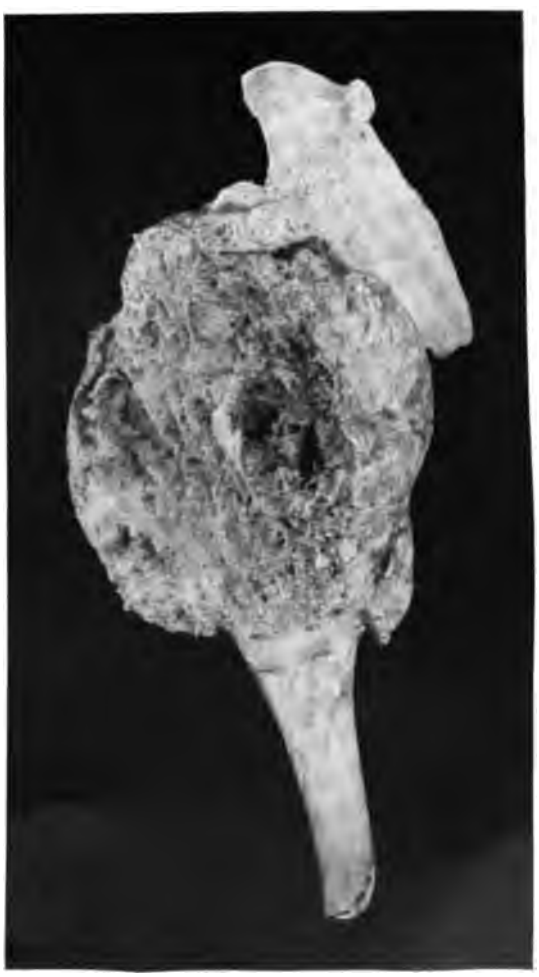


Fig. 31.—Innocent Osteoma of Humerus (No. 2)
Section

SECOND GRADATION SERIES—*Continued*

Fig. 32.—Large Osteofibroma of Ulna (No. 3)

Fig. 33. –Enormous Fibro-osseous Tumour of Jaw (No. 4)

SECOND GRADATION SERIES—*Continued*

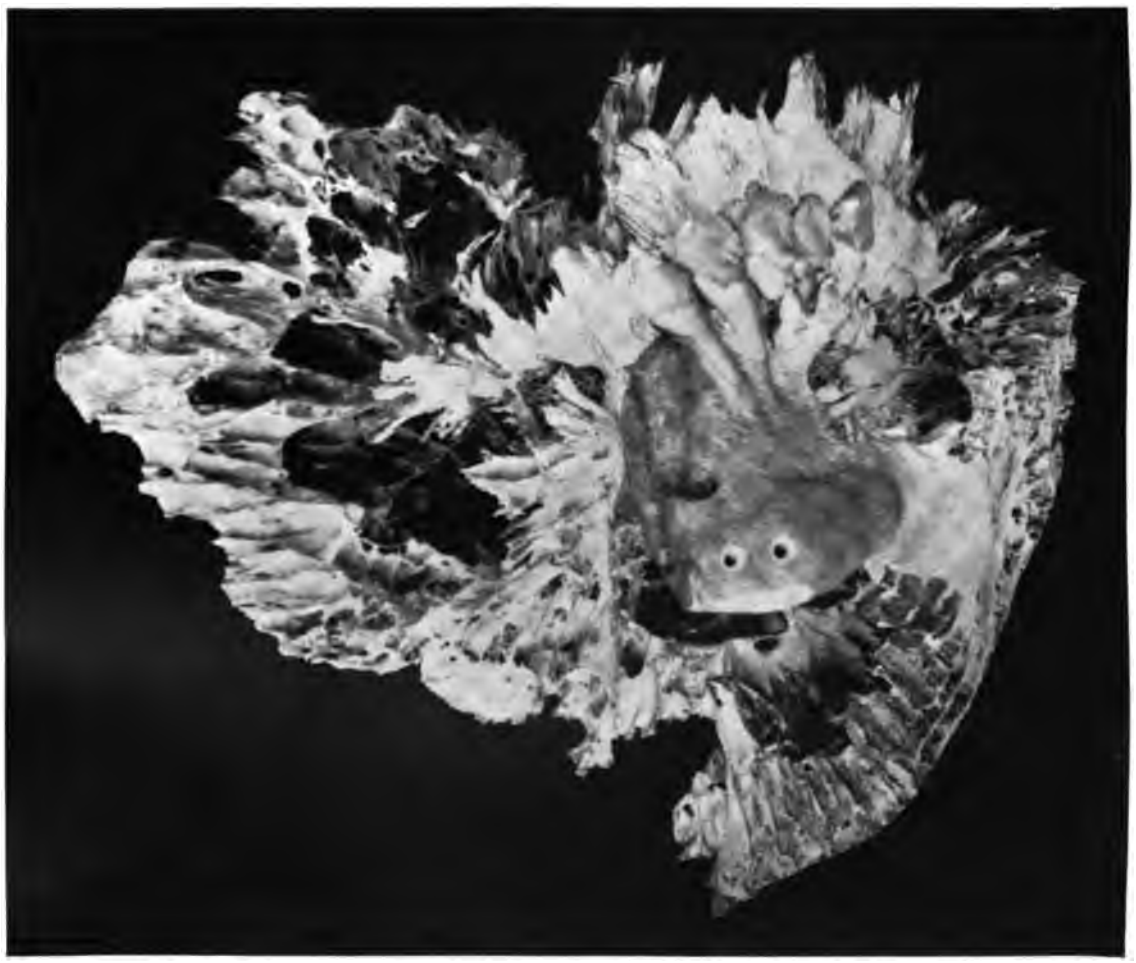


Fig. 34.—Enormous Fibro-osseous Tumour of Jaw (No. 4). Front view

SECOND GRADATION SERIES—*Continued*

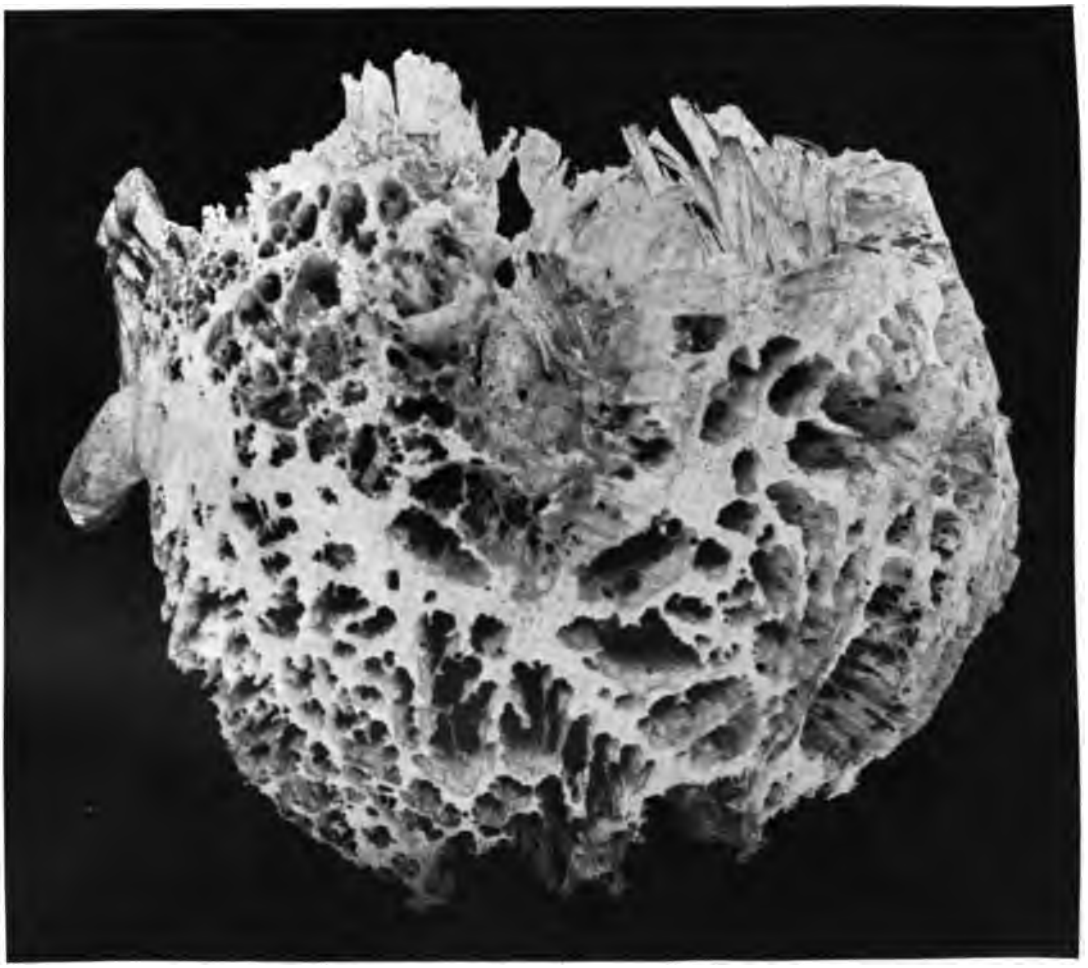


Fig. 35.—Enormous Fibro-osseous Tumour of Jaw (No. 4). Side view

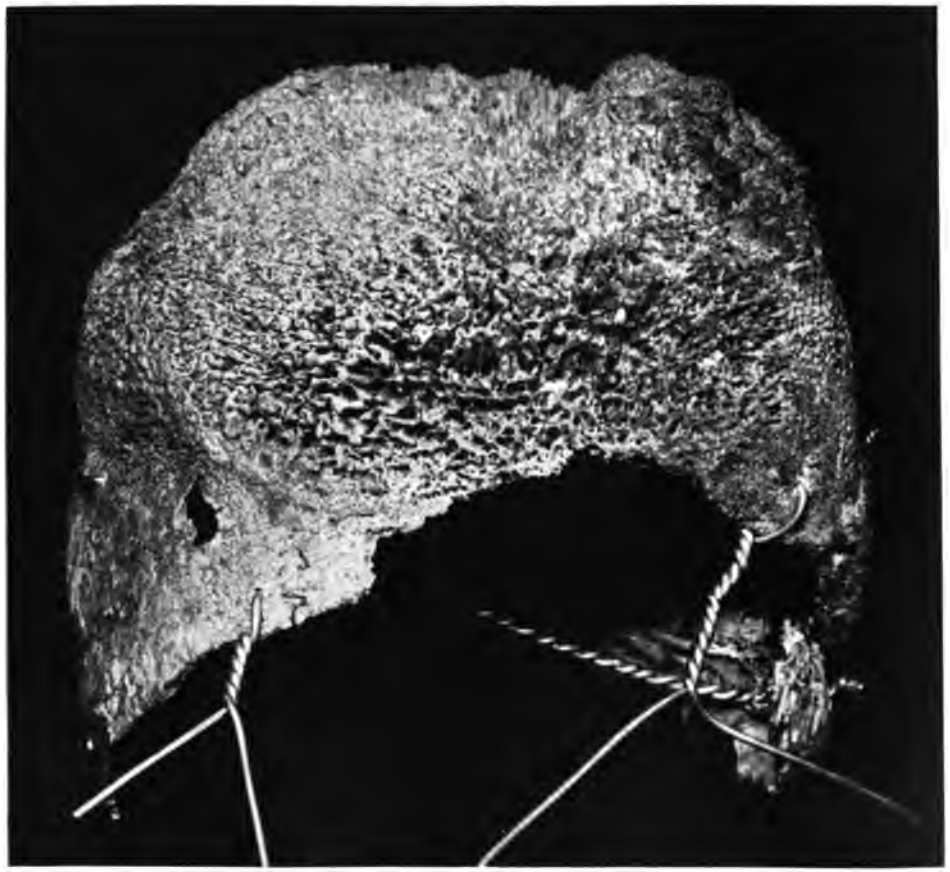


Fig. 36.—Osteosarcoma of Skull (No. 5)

Fig. 37.—Osteosarcoma of Femur—Spontaneous Fracture (No. 6)

SECOND GRADATION SERIES—*Continued*

Fig. 38.—Osteofibroma of Femur (No. 7)

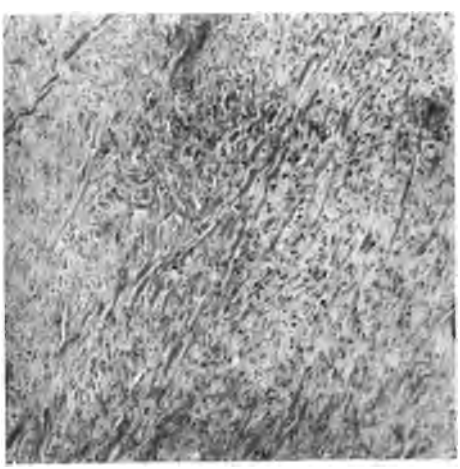


Fig. 39.—Photomicrograph of (No. 7)

SECOND GRADATION SERIES—*Continued*

Fig. 40.—Osteofibroma of Femur (No. 7). Macerated outer surface

SECOND GRADATION SERIES—*Continued*

Fig. 41.—Osteofibroma of Femur (No. 7). Macerated cut surface

Fig. 42.—Recurrent osseous Tumour of Femur (No. 8). Original Tumour

Fig. 43.—Recurrent osseous Tumour of Femur (No. 8) Recurrence in stump of first amputation

SECOND GRADATION SERIES—*Continued*

Fig. 44.—Cystic Osteosarcoma of Femur (No. 9)

Fig. 45.—Osteosarcoma of Tibia (No. 10)

SECOND GRADATION SERIES—*Continued*

Fig. 46.—Osteosarcoma of Femur (No. 11)

Fig. 47.—Osteosarcoma of Femur (No. 11)

SECOND GRADATION SERIES—*Continued*

Fig. 48.—Osteosarcoma of Femur (No. 11)
Recurrence in Stump of Femur

Fig. 49.—Osteosarcoma of Femur (No. 11)
Recurrence in Stump of Femur

Fig. 50.—Osteosarcoma of Femur (No. 12)

Fig. 51.—Periosteal Sarcoma of Femur (No. 13)

SECOND GRADATION SERIES—*Continued*

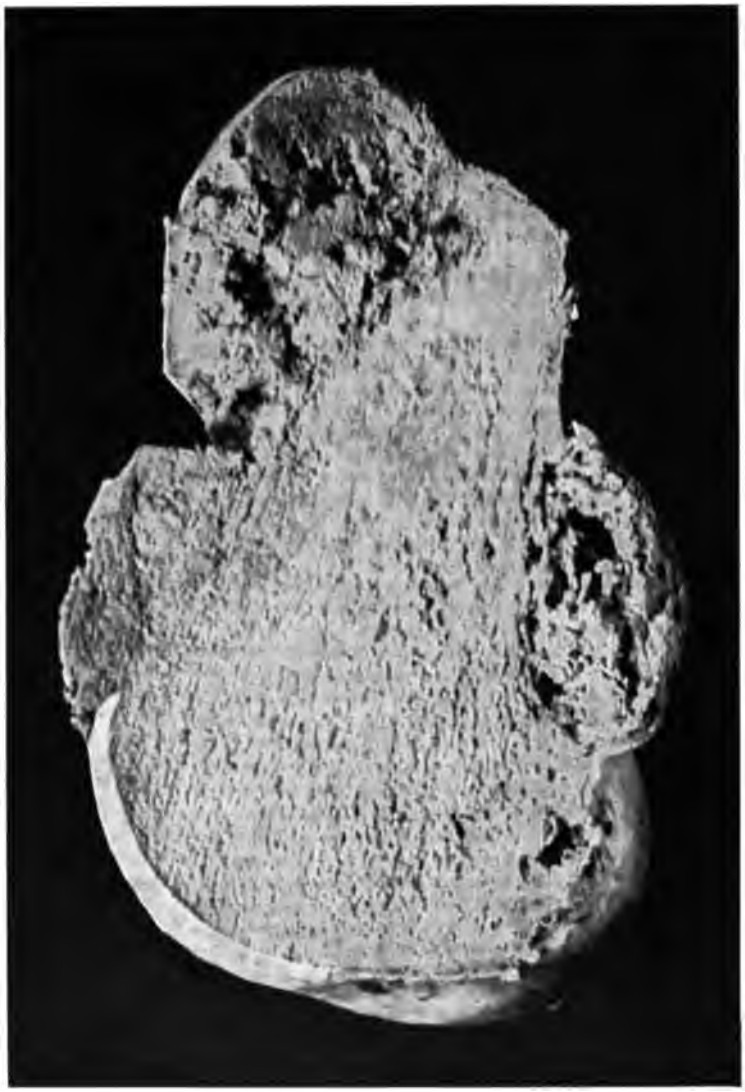


Fig. 52.—Periosteal Sarcoma of Femur (No. 14)

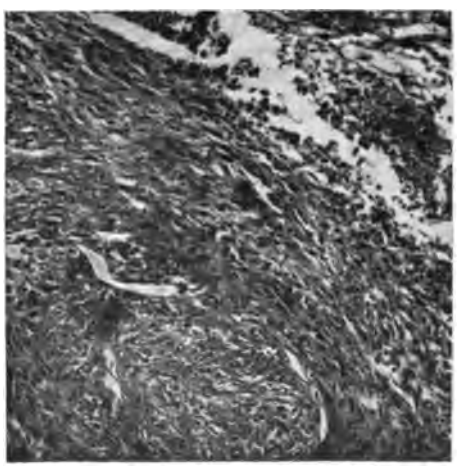


Fig. 53.—Photomicrograph of (No. 14) Firmer part

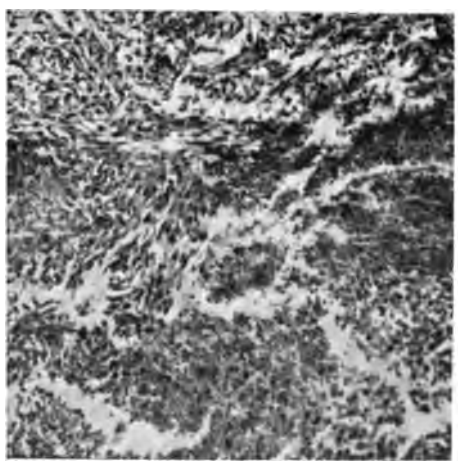


Fig. 54.— Photomicrograph of (No. 14) Softer part

SECOND GRADATION SERIES—*Continued*

Fig. 55. Periosteal Sarcoma of Femur (No. 15) From cast

Fig. 56.—Periosteal Sarcoma of Femur (No. 15) Section

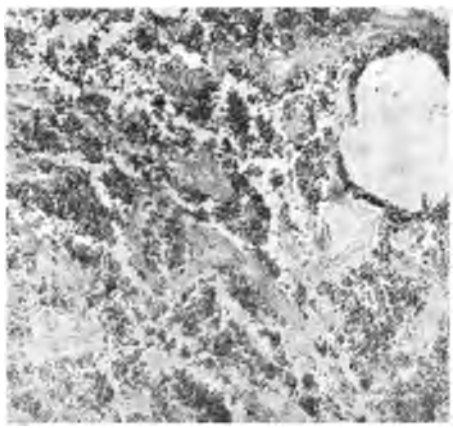


Fig. 57.—Photomicrograph of (No. 15)

SECOND GRADATION SERIES—*Continued*

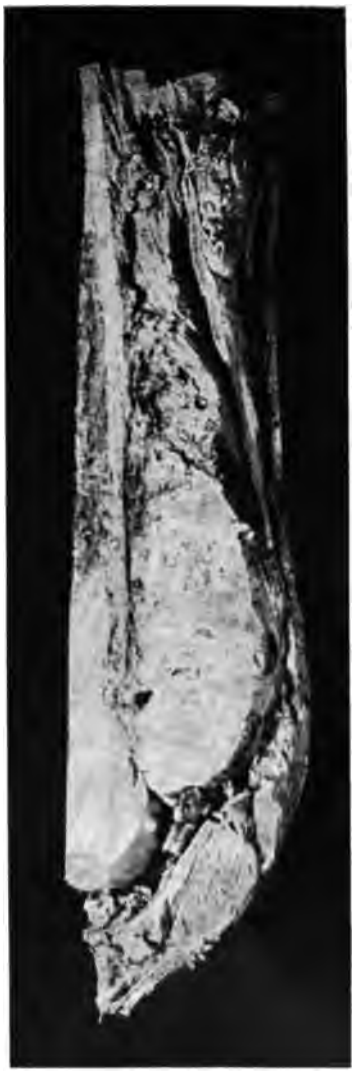


Fig. 58.—Periosteal Sarcoma of Femur (No. 16)

Fig 59 —Periosteal Sarcoma of Femur (No. 16) Part of the Femur macerated

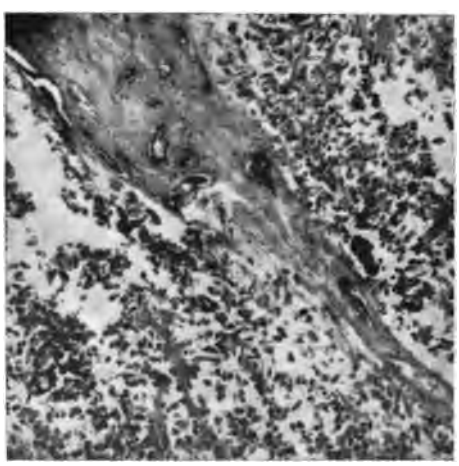


Fig. 60.—Photomicrograph of (No. 16)

THIRD GRADATION SERIES

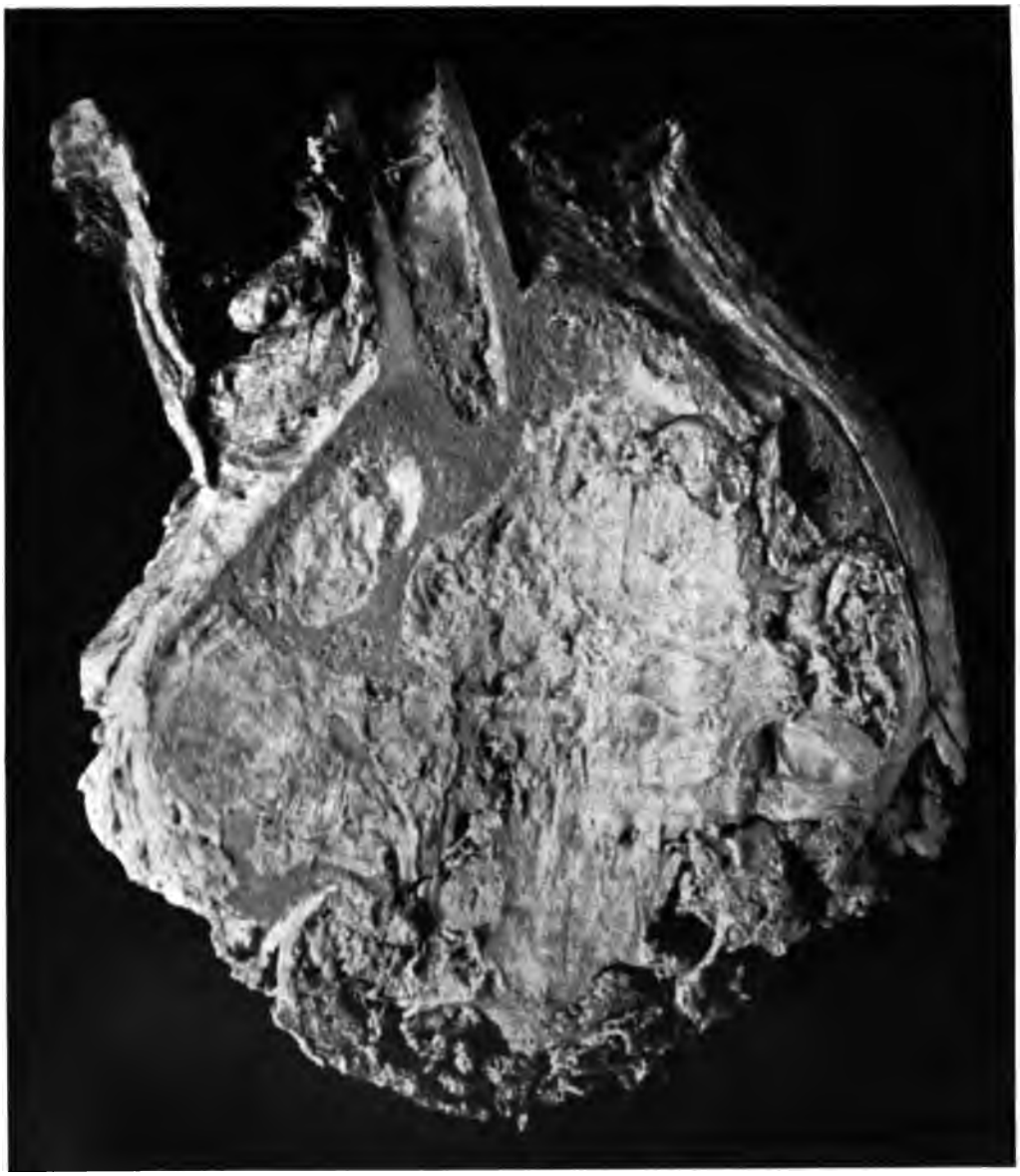


Fig. 61.—Large Central Tumour of Lower End of Femur (No. 1)

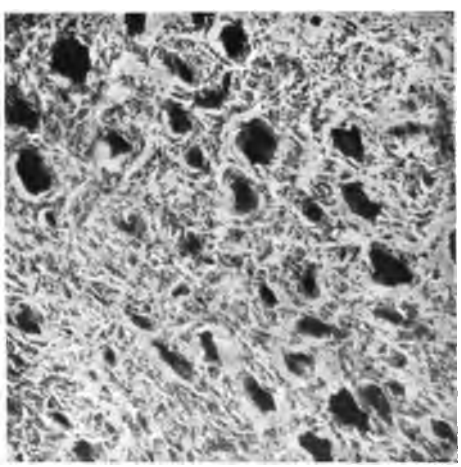


Fig. 62.—Photomicrograph of (No. 1)

THIRD GRADATION SERIES—*Continued*

Fig. 63.—Innocent Myeloid Tumour of Lower Jaw (No. 2)

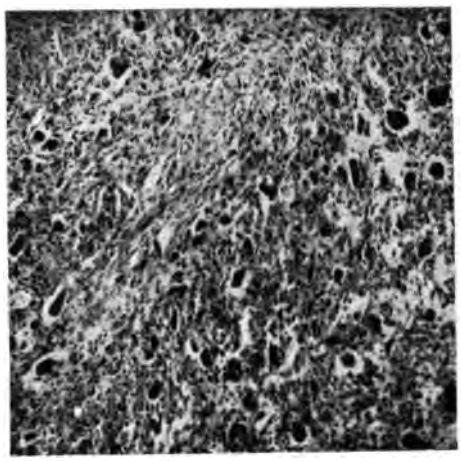


Fig. 64.—Photomicrograph of (No. 2)

Fig. 65.—Innocent Myeloid Tumour of Humerus (No. 3)

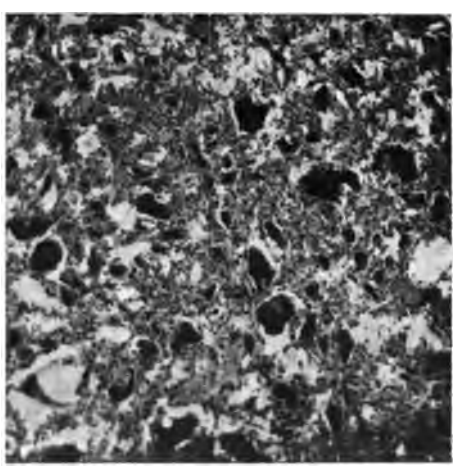


Fig. 66.—Photomicrograph of (No. 3)

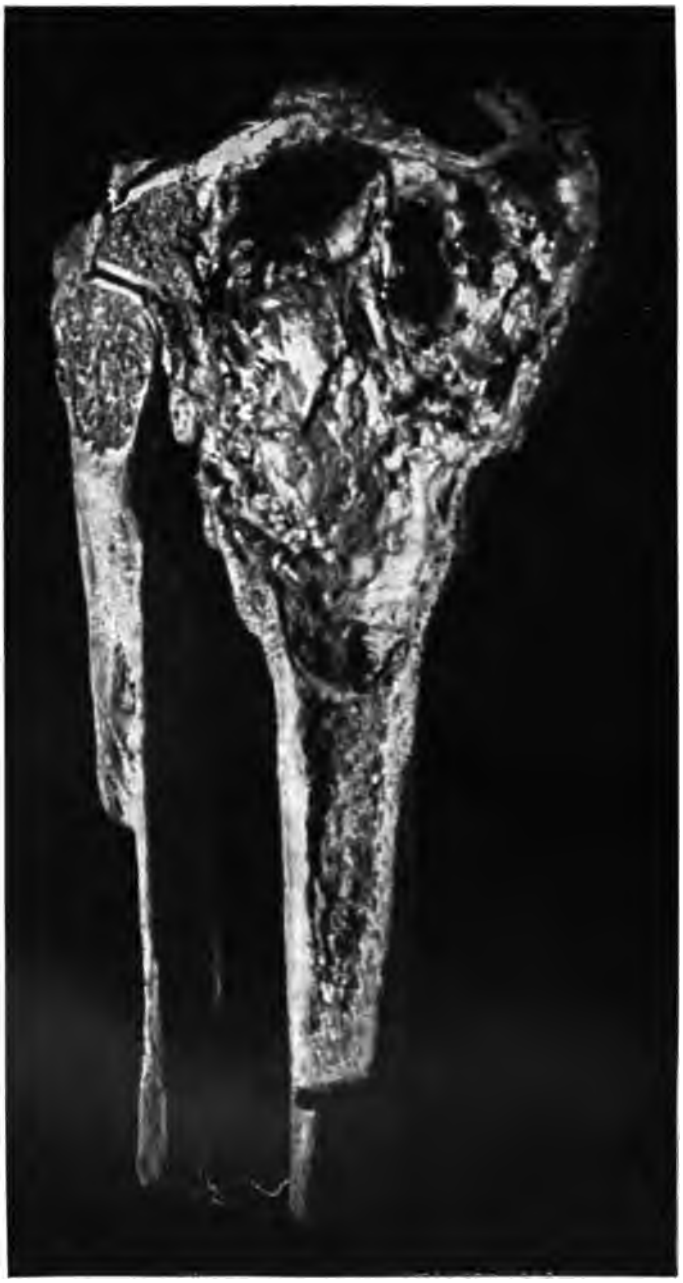


Fig. 67. Myeloid Tumour of Head of Tibia (No. 4)

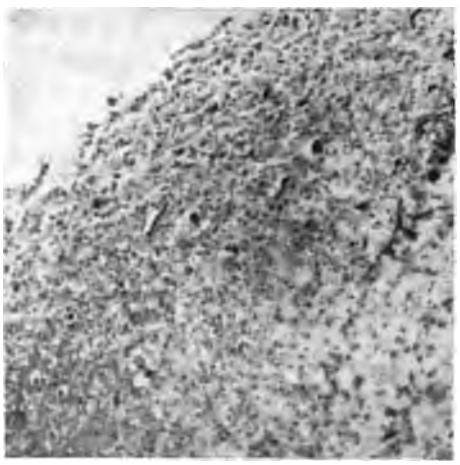


Fig. 68.—Photomicrograph of (No. 4)

THIRD GRADATION SERIES—*Continued*

Fig. 69.—Central Tumour of Tibia, probably Myeloid (No. 5)

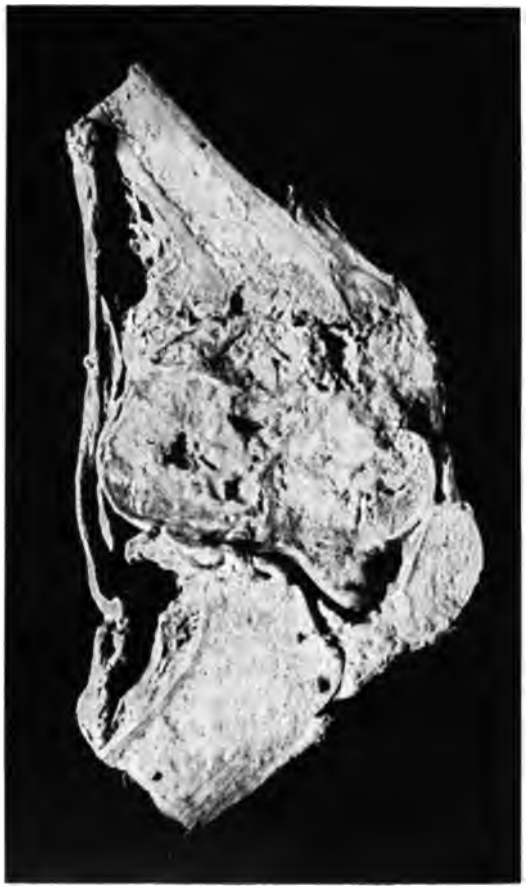


Fig. 70.—Locally Malignant Myeloid Tumour of Femur (No. 6)

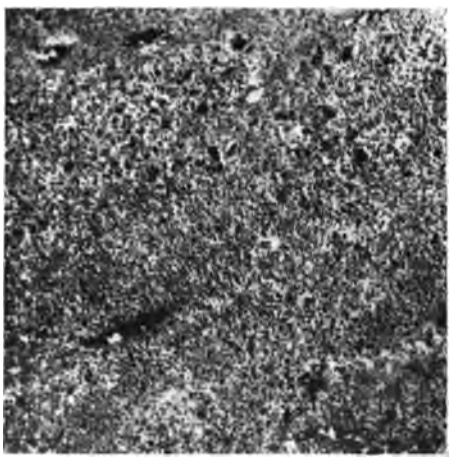


Fig. 71.—Photomicrograph of (No. 6)

THIRD GRADATION SERIES—*Continued.*

Fig. 72.—Fungating Myeloid Tumour of Lower End of Humerus (No. 7). From Cast

Fig. 73.—Fungating Myeloid Tumour of Lower End of Humerus (No. 7)

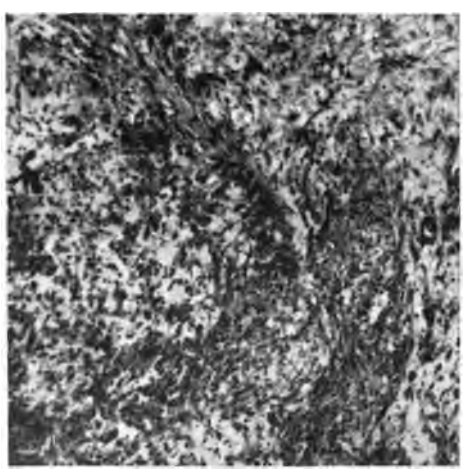


Fig. 74.—Photomicrograph of (No. 7)

THIRD GRADATION SERIES—*Continued*

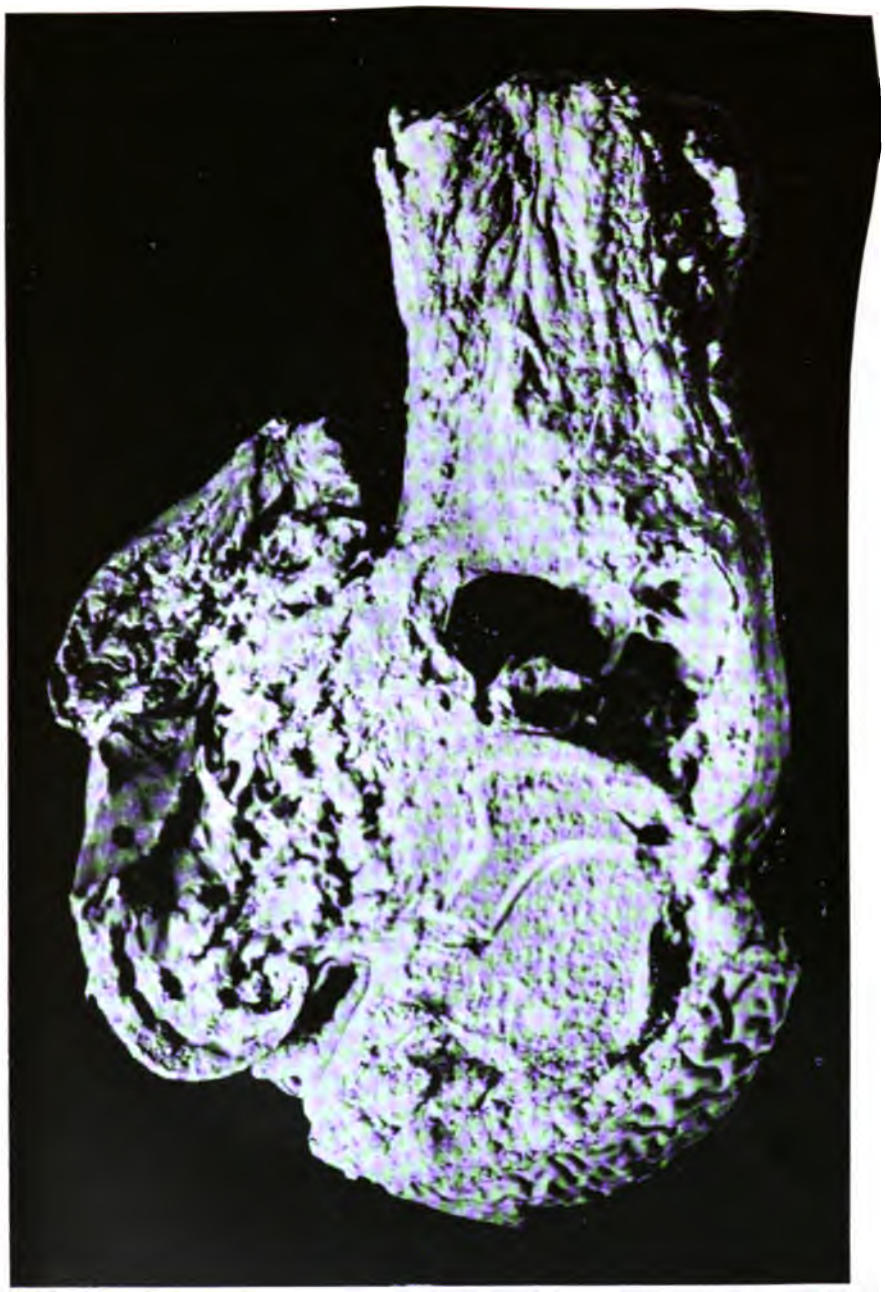


Fig. 75.—Fungating Tumour of Tibia (No. 8)

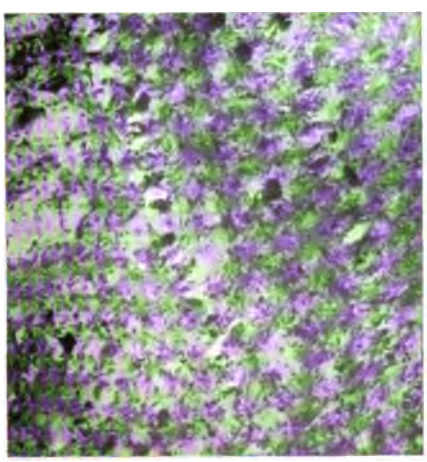


Fig. 76.—Photomicrograph of (No. 8)

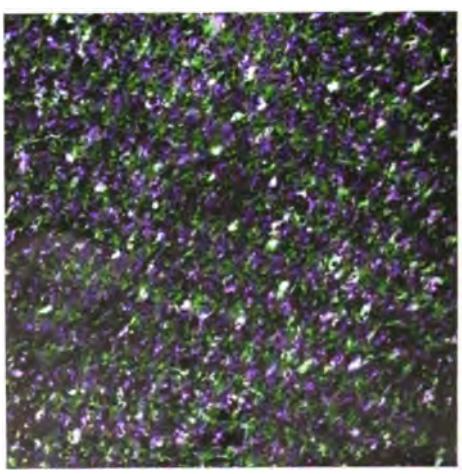


Fig. 77.—Photomicrograph of (No. 8)

THIRD GRADATION SERIES—*Continued*

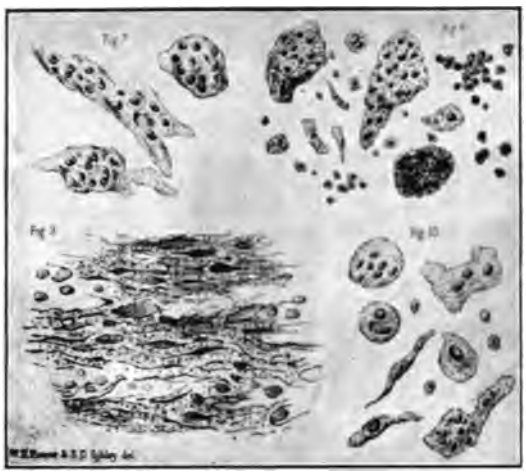


Fig. 78.—From Trans. Path. Soc. London, Vol. ix. (No. 11)

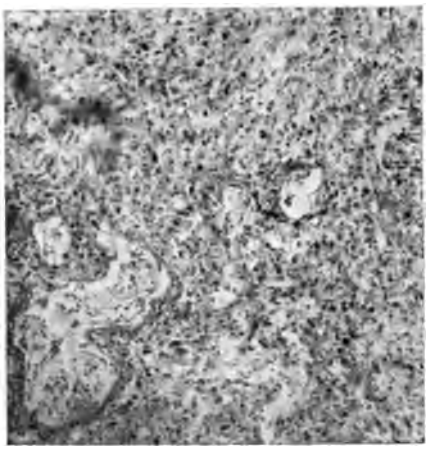


Fig. 79.—Photomicrograph of (No. 12)

Fig. 80.—Central Sarcoma of Head of Tibia (No. 12)

THIRD GRADATION SERIES—*Continued*

Fig. 81.—Central Sarcoma of Femur (No. 13)

Fig. 82.—Central Sarcoma of Femur (No. 13) Macerated portion

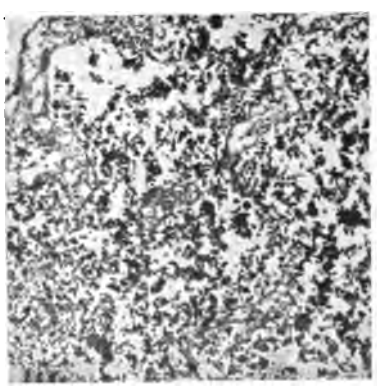


Fig. 83.—Photomicrograph of (No. 13)

THIRD GRADATION SERIES—*Continued*

Fig. 84.- Sarcoma of Head of Tibia (No. 14)

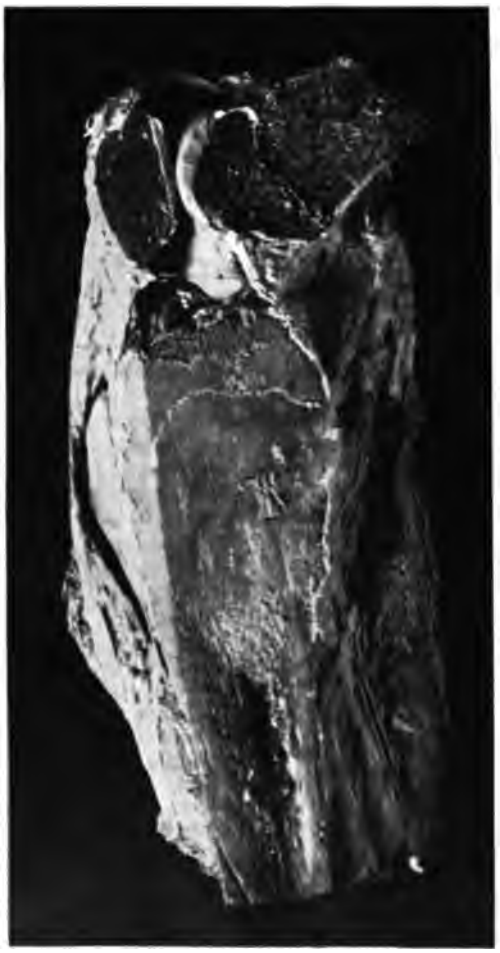


Fig. 85.- Sarcoma of Tibia (No. 14)

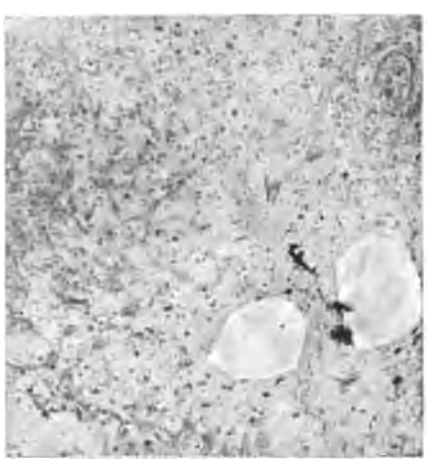


Fig. 86. -Photomicrograph of (No. 14)